’GRACIOUS blueprint’

version 1.0

Intelligent Objects

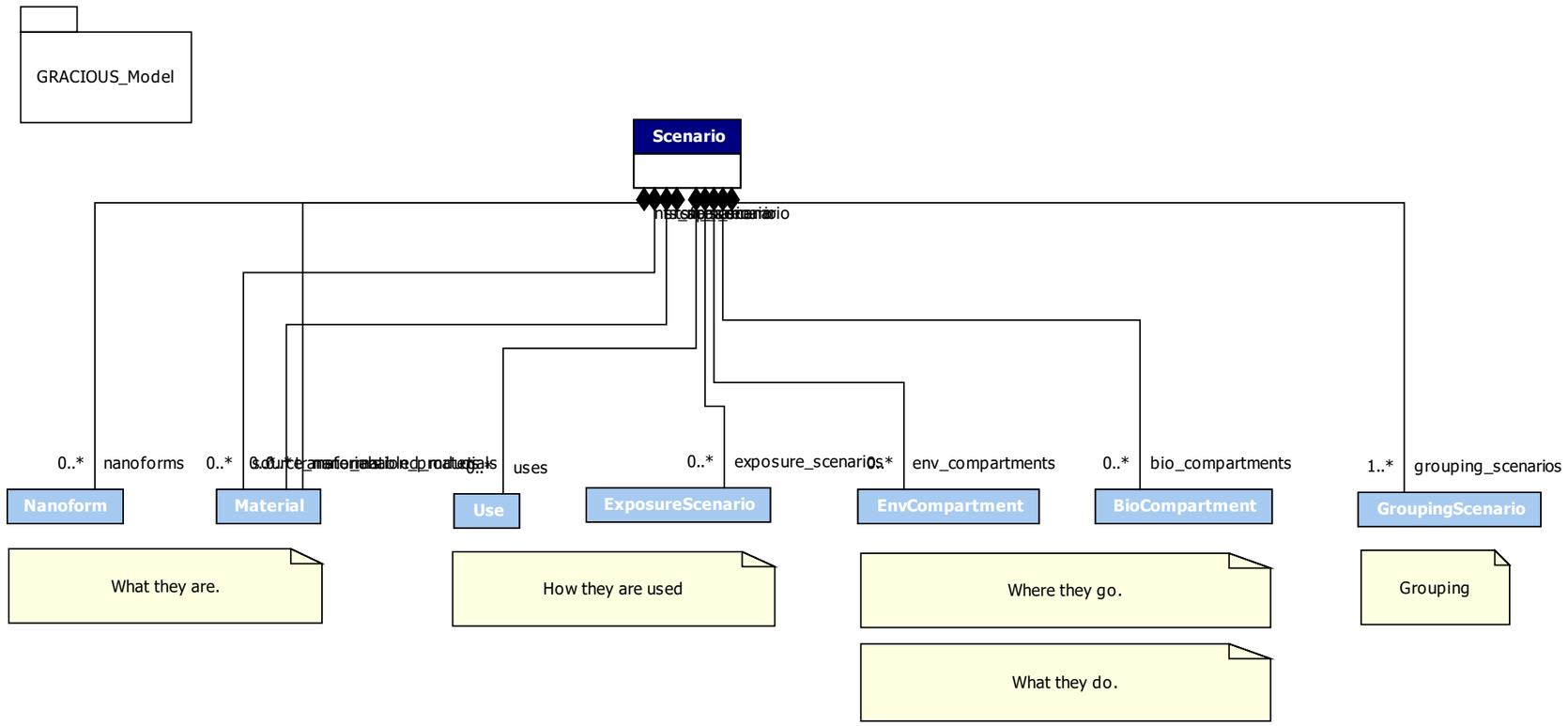
28 September 2021 12:30

Contents

Abstract

This is version 1.0 of the GRACIOUS framework blueprint.
PLEASE NOTE! THIS DOCUMENT IS AUTOMATICALLY GENERATED.
PLEASE REPORT YOUR COMMENTS, ADDITIONS, SUGGESTIONS via https://gitlab.com/h2020gracious
Wiki : https://terminology-harmonizer.greendecision.eu/Gracious

Chapter 1 GRACIOUS_Model



1.1 Defined classes

Class `Scenario`

A scenario represents the case to be assessed. It's the root-object and the outer context for the entire assessment. The scenario contains all the materials, compartments, use descriptions, etc required to conduct the assessment.

Attributes

name	type	domain	inference	comment
`name`	: `String`			*A name in order to identify this specific scenario.*
`description`	: `String`			*A brief description of the scenario to be assessed.*
`knowledgebase_datetime`	: `DateTime`			*The datetime of the knowledgebase most recently used for this scenario. (Used to update the scenario in case of knowledgebase updates).*
`created`	: `DateTime`			*The datetime this scenario is created.*
`last_modified`	: `DateTime`			*The datetime this scenario was last modified.*
`purpose`	:: `GroupingPurpose`			*The main purpose of the assessment, (precautionary, safe-by-design, regulatory)*

Defined composites

Any instance of `Scenario` is composed of

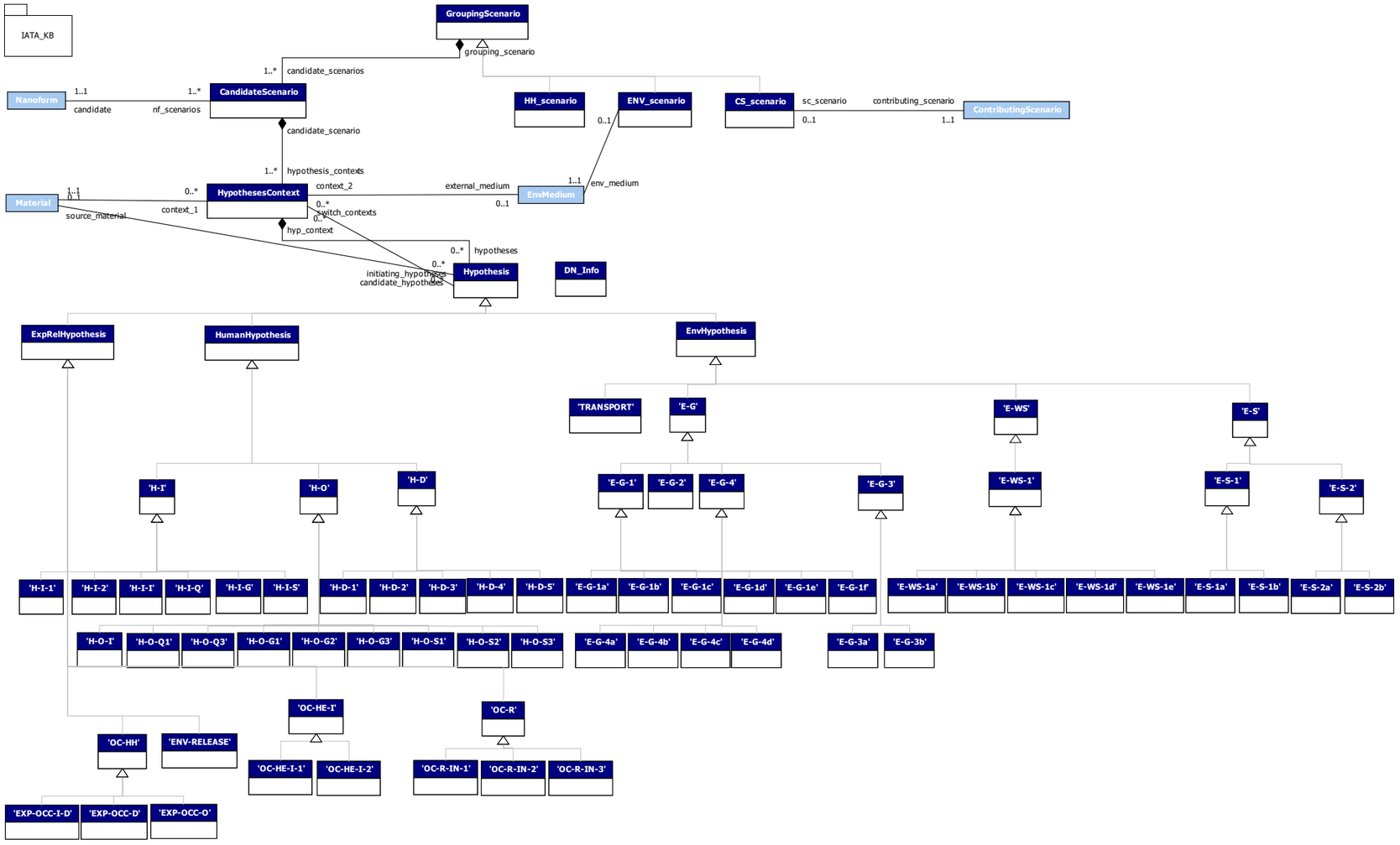
- zero or more `source_materials` of any kind of Material *The source materials to be used within the scenario, either provided by the user or loaded from a database like (eNanoMapper)*
- zero or more `env_compartments` of any kind of EnvCompartment *The compartments relevant for this case like system compartments (indoor air, etc) or environmental compartments like soil, freshwater.*
- zero or more `bio_compartments` of any kind of BioCompartment *Biocompartments are specific populations who act as receptors in use/exposure scenarios.*
- zero or more `nanoforms` of Nanoform *The candidate nanoforms to be grouped.*
- zero or more `transformation_products` of any kind of Material *The molecules/ ions and transformed nanoforms as a result of processes transforming or dissolving the candidate nanoforms.*
- zero or more `uses` of Use *The different use scenarios the candidate nanoforms are assessed for.*
- zero or more `exposure_scenarios` of ExposureScenario *The use corresponding exposure scenarios the candidate nanoforms are to be assessed for.*
- zero or more `nano_enabled_materials` of any kind of Material *The products/substances and articles the candidate nanoforms are enabled with. To be used as part of the use description. And relevant in the exposure/release IATAs.*
- one or more `grouping_scenarios` of any kind of GroupingScenario *The different scenarios for grouping the candidate nanoforms, either via an exposure scenario or direct via an assumed route of exposure or environmental release compartment.*

1.2 Defined composites

Any instance of `GRACIOUS_Model` is composed of

- zero or more `scenarios` of Scenario *This composite holds the loaded case (Scenario-object)*

Chapter 2 IATA_KB



The IATA knowledgebase contains a set of classes representing the IATAs developed within the GRACIOUS framework.

2.1 Defined enumerations

`GroupingPurpose`

The purpose/reason for grouping. (See GRACIOUS D4.2)

- `'precautionary'`
- `'safe-by-design'`
- `'regulatory'`

`HypothesisOutcome`

Used to indicate the state of IATA evaluation.

- INCL
  The considered material has been 'included' based upon the the grouping rules in the hypothesis.
- EXCL
  The considered material has been 'excluded' based upon the the grouping rules in the hypothesis.
- UND
  The considered material cannot be 'included' or 'excluded' based upon the grouping rules in the hypothesis. (?)
- MI
  The considered material cannot be grouped because not all information needed to apply the grouping rules in the hypothesis is available (yet).
- IRR
  The hypothesis is irrelevant for the context
- NYI
  The hypothesis is not yet implemented.

YesNo

Used as decision node outcome.

- Yes
- No

TierLevel

The IATAs follow a tiered approach per decision node within them. Each tier level represents a level of confidence/certainty the information provides to determine the outcome of a decision node.

- TL1
  Tier 1, is the lowest tier level mostly used as a screening level, either with conservative outcomes, or outcomes with the higher level of uncertainty.
- TL2
  Tier 2, information/data and assays used at tier2 provide a higher level of confidence for the decision node outcome, however are often more costly.
- TL3
  Tier 3, provides the highest level of confidence for the decision node outcome. The results are often based on in vivo studies or experiments in actual relevant media.

ContextSwitchReason

Each IATA is evaluated within a fixed context. The context is determined by the target material and the environmental medium in case of environmental IATAs. In case the target material dissolves/transformes and/or moves to another medium due to transport processes a context switch occurs.
A context switch creates a new evaluation context and contains and triggers its own relevant IATAs to be assessed.
This enumeration is used to indicate the cause of that context switch.

- coMaterialReadAcross
  Conceptual, read across of the target material to another source material.
- coMediumReadAcross
  Conceptual, would allow read across from a target medium towards a source medium.
- coExposureReadAcross
  Conceptual, would allow read across from existing exposure conditions to a source exposure scenario. (e.g. read across of exposure concentration estimation etc.)
- coChemicalReadAcross
  Read across of target material to a chemical (either molecule or ionic form)
- coUncoatedReadAcross
  Read across of target nanomaterial to an equivalent nanomaterial without the coating(s) applied.
- coSettleProcess
  The context switch is caused by transport of the target material between two media due to gravitational settling. (e.g. river water to river sediment)
- coTransformationProcess
  The context switch is caused by the transformation of the current target material into a new target material as a result of speciation reactions with within the surrounding environmental mediium.
- coDissolutionProcess
  The context switch is caused by dissolution of the target material into solutes (ions/molecules) within the same environmental medium.
- coTransportProcess
  A context switch caused by an advection process transporting the target material from one environmental zone towards another zone.

GroupDescriptor

- 'NF is respirable, biopersistent, rigid HARN with potential to cause lung hazard'
- 'NF is respirable, biopersistent, rigid HARN with potential to cause mesothelioma'
- 'NF aquatic toxicity is driven by the fate and toxicity characteristics of the solutes'
- 'NF aquatic toxicity is driven by the fate and toxicity characteristics of the NF in aquous environment'
- 'NF dissolves instantaneous in OGI fluids'
- 'NF dissolves quick in OGI fluids'

- 'None biopersistent NF dissolves quick in OGI fluids'
- 'NF dissolves gradually in OGI fluids'
- 'Biopersistent and systemic toxic NF and/or constituent ions or molecules'
- 'Highly biopersistent NF and chronic systemic toxic'
- 'NF dissolves very slow in OGI fluids'

ContextType

Type of evaluation context.

- ctHH
  Direct human health, start context for inhalation, oral, dermal IATA. (No use description required)
- ctEnv
  Direct envirionmental compartment start context. Allows IATAs to be triggered for a certain selected environmental compartment without a use description.
- ctCS
  The context is determined by a 'contributing scenario' as part of an 'exposure scenario'. Depending on the perspective of the contributing scenario certain 'exposure IATA's are triggered'. The outcome of these exposure IATAs trigger the relevant human health or environmental IATA's (Note only a few exposure IATAs have been implemented)
- ctSwitch
  Indicates that the current context is not a starting context but caused by a switch action.

ScenarioType

Indicates if the grouping scenario is related to human health or environemental grouping scenario.

- stHuman
- stEnvironment

Section

Used to indicate the section a decision node or endpoint qualifier belongs to.

- sWTA
  What They Are
- sWTL
  Where They Leave
- sWTG
  Where They Go
- sWTD
  What They Do

2.2 Defined classes

Class GroupingScenario

A grouping scenario is an abstract class representing three classes (ways) to determine the grouping context.
One of the scenarios used for grouping.

Attributes

name	type	domain	inference	comment
name	: String			*To provide a name for this grouping scenario by the user.*

Defined expressions

name	type	expression	comment
type_name	: String	"grouping scenario"	*Abstract grouping scenario type name.*
perspective	:: CA_Perspective	**nil**	
context_type	:: ContextType	**nil**	
scenario_type	:: ScenarioType	**nil**	
relevant_medium	: EnvMedium	**nil**	

Operators

```
function GroupingScenario.GetEquivalentHypothesis( h : Hypothesis ): Hypotheses
  foreach cs of candidate_scenarios do
    with cs.GetEquivalentHypothesisContext(h.hyp_context) | eq_hc then
    begin
      with eq_hc.hypotheses→Any(hyp | hyp is h→Type) | eq_hyp then
        result→Add(eq_hyp)
    end
```

Defined composites

Any instance of GroupingScenario is composed of
- one or more candidate_scenarios of CandidateScenario

Class CS_scenario is kind of GroupingScenario

A scenario derived based upon a contributing scenario described as part of the basic information use description.

Defined expressions

name	type	expression	comment
type_name	: String	"CS scenario"	*A contributing exposure scenario is used as context for the hypothesis.*
perspective	: CA_Perspective	contributing_scenario→**If**(cs | cs.ca_perspective, **nil**)	
context_type	: ContextType	ctCS	
scenario_type	: ScenarioType	DeriveScenarioType()	
relevant_medium	: EnvMedium	DeriveMedium()	

Operators

function CS_scenario.DeriveScenarioType(): ScenarioType

C1	contributing_scenario	nil	ELSE		
C2	contributing_scenario.ca_perspective | p	-	occupational,consumer	environmental	ELSE
A1	result	nil	stHuman	stEnvironment	nil
		R1	R2	R3	R4

function CS_scenario.DeriveMedium(): EnvMedium

C1	contributing_scenario | cs	nil	ELSE			
C2	cs.env_comp | cmp	-	nil	ELSE		
C3	cmp.zones | zones	-	-	0	1	ELSE
A1	result	nil	nil	nil	zones[1].medium	nil
		R1	R2	R3	R4	R5

Class `HH_scenario` is kind of `GroupingScenario`

A direct scenario for Human Health hazard endpoints.

Attributes

name	type	domain	inference	comment
primary_exposure_route	:: ExposureRoute			

Defined expressions

name	type	expression	comment
type_name	: String	"HH scenario"	
context_type	: ContextType	ctHH	
scenario_type	: ScenarioType	stHuman	

Class `ENV_scenario` is kind of `GroupingScenario`

A direct scenario for envirionmental hazard endpoints.

Defined expressions

name	type	expression	comment
type_name	: String	"Env scenario"	
perspective	: CA_Perspective	environmental	
context_type	: ContextType	ctEnv	
scenario_type	: ScenarioType	stEnvironment	
relevant_medium	: EnvMedium	env_medium	

Operators

```
function ENV_scenario::Potential_EnvCompartmentClasses() :: EnvCompartmentClasses
| EnvCompartmentClasses{WWTP, FreshWater, MarineWater, Soil, FreshWaterSediment}


function ENV_scenario.OnNew_EnvironmentalCompartment(ec_class :: EnvCompartment ): EnvMedium
  with scenario.Add_EnvCompartment(ec_class) | newEnvCompartment then
  begin
    result := newEnvCompartment.zones[1].medium
  end
```

Class `CandidateScenario`

The candidate scenario represents one of the candidate nanoforms within the grouping scenario. The candidate scenario owns the initial context and the context switches related to

Defined expressions

name	type	expression	comment
scenario	: Scenario	grouping_scenario.scenario	
cs	: ContributingScenario	(grouping_scenario **is** CS_scenario)→**If**((grouping_scenario **as** CS_scenario).contributing_scenario, **nil**)	
context_type	:: ContextType	grouping_scenario.context_**type**	
scenario_type	:: ScenarioType	grouping_scenario.scenario_**type**	
scenario_medium	: EnvMedium	grouping_scenario.relevant_medium	*The initial medium the scenario starts with.*

Operators

```
function CandidateScenario.SpeciationInMedium( env_medium : EnvMedium ): Materials
  if env_medium ≠ nil then
    with hypothesis_contexts→Select(hc | hc.medium = env_medium) | relevant_contexts then
      result := relevant_contexts.material→Select(m | m ≠ nil)→Unique


function CandidateScenario.GetEquivalentHypothesisContext( hc : HypothesesContext ): HypothesesContext
  begin
    /*  */  ;
    if hc.is_start_context then
      result := hypothesis_contexts→Any(hc2 | hc2.is_start_context)
    else
      result := hypothesis_contexts→Any(hc2 | (hc2.medium = hc.medium) and (hc2.material = hc.material))
  end
```

Defined composites

Any instance of `CandidateScenario` is composed of

- one or more `hypothesis_contexts` of HypothesesContext

Class `HypothesesContext`

The context for evaluation of the different hypotheses. A context object is a component of a candidate scenario, which is related to one of the candidate nanoforms for evaluation. All candidate scenarios own an 'initial' context object. Every context object instantiates all the potential predefined hypotheses. The information coming from the context object is used to determine which hypotheses are to be triggered. A context object may contain information on the likely routes of exposure, the target material and the surrounding medium. If the context is expected to change, a 'new' context object is instantiated including a new 'empty' set of hypothesis. This is called a 'context switch'.

A 'context switch' basically means that we either expect the target material to change or its surrounding medium due to (environmental) processes. A series of sequential context switches may occur for instances when nanoparticles transform / dissolve and/or are transported to other environmental compartments.

Attributes

name	type	domain	inference	comment
name	: String			
description	: String			
expected_routes	: ExposureRoutesSet		Infer routes of exposure	

Inference methods

Inference method: 'Infer routes of exposure'

C1	context_type	ctHH			ctCS		ELSE	
C2	contributing_scenario | cs	-			nil	ELSE	-	
C3	candidate_scenario.grouping_scenario as HH_scenario | hhsc	nil	ELSE		-	-	-	
C4	hhsc.primary_exposure_route | per	-	nil	ELSE	-	-	-	
A1	expected_routes					cs.likely_routes_of_exposure		
A2	expected_routes→Add(per)			X				
		R1	R2	R3	R4	R5	R6	

Defined expressions

name	type	expression	comment
relevant_hypotheses	: Hypotheses	DeriveRelevantHypotheses()	
is_start_context	: Boolean	original_context = **nil**	*Indicates that this context is the initial context before any context-switches has taken place.*
original_context	: HypothesesContext	GetOriginalContext()	*The original context is the context which caused the context to switch towards this one. Currently hypothesis within the same original context and with the same switch action are allowed.*
action	:: ContextSwitchReason	GetSwitchAction()	
medium	: EnvMedium	DeriveMedium()	
scenario	: Scenario	candidate_scenario→**If**(csc | csc.scenario, **nil**)	
contributing_scenario	: ContributingScenario	candidate_scenario.cs	*Shortcut expression, returns the contributing scenario of the*
context_type	:: ContextType	is_start_context→**If**(candidate_scenario.context_**type**, ctSwitch)	
scenario_type	:: ScenarioType	candidate_scenario.scenario_**type**	
env_compartment	: EnvCompartment	medium→**If**(m | m.zone→**If**(z | z.compartment, **nil**), **nil**)	
relevant_switch_causes	: SwitchCauses	relevant_hypotheses→Collect(hyp | hyp~switch_contexts)→Sum	
speciation	: Materials	candidate_scenario.SpeciationInMedium(medium)	

Operators

```
constructor HypothesesContext.Create()
  with self→New | newHypothesisContext do
  begin
    result := newHypothesisContext;
    result→SynchronizeComponents(hypotheses, Hypothesis→Leaves)
  end


function HypothesesContext.SwitchContext(): HypothesesContext
  with HypothesesContext.Create() | newContext then
  begin
    candidate_scenario→AddComponent(hypothesis_contexts, newContext);
    result := newContext
  end


function HypothesesContext.GetOriginalContext(): HypothesesContext
  with self~initiating_hypotheses | switch_causes then
    if (switch_causes.action→Unique→Size = 1) and (switch_causes.initiating_hypotheses→Unique→Size = 1) then
      result := switch_causes[1].initiating_hypotheses.hyp_context
```

```
function HypothesesContext.GetSwitchAction(): ContextSwitchReason
  with self~initiating_hypotheses | switch_causes then
  begin
    if (switch_causes.action→Unique→Size = 1) then
      result := switch_causes[1].action
  end
```

```
function HypothesesContext.GetInMedium(): medium_interaction
  with material | matr then
    with medium | med then
      with matr~relevant_media→Any(r | r.relevant_media = med) | rel then
        result := rel
      else
        with medium_interaction→New | rel then
        begin
          rel.relevant_materials := matr;
          rel.relevant_media := med;
          result := rel
        end
```

```
function HypothesesContext.DeriveRelevantHypotheses(): Hypotheses
  begin
    if contributing_scenario ≠ nil then
      contributing_scenario.Reset_Status()  ;
   result := hypotheses→Select(h | h.DetermineOutcome() ≠ IRR)
  end
```

```
function HypothesesContext.DeriveMedium(): EnvMedium
```

C1	context_type	ctHH	ctEnv,ctCS	ctSwitch					
C2	external_medium	-	-	nil					ELSE
C3	initiating_hypotheses	-	-	nil		ELSE			-
C4	self~initiating_hypotheses.action	-	-	-		coSettleProcess, coTransportProcess	ELSE		-
C5	contributing_scenario	-	-	nil	ELSE	-	nil	ELSE	-
A1	result	external_medium	candidate_scenario.scenario_medium	nil	contributing_scenario.medium	nil	initiating_hypotheses[1].hyp_context.medium	contributing_scenario.medium	external_medium
		R1	R2	R3	R4	R5	R6	R7	R8

Defined composites

Any instance of `HypothesesContext` is composed of

- zero or more `hypotheses` of any kind of Hypothesis

Class `Hypothesis`

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate.
The 'leave' classes of the hypothesis hierarchy are the actual predefined hypotheses as described in the GRACIOUS framework.
As they also contain information on the tiered testing strategies for the decision nodes in them they are also calles IATAs (Integrated Approach for Testing and Assessment).
Each of them implements a specific decision table to derive the outcome based on the decision nodes. (see function(s) DeriveOutcome()).
The tiered testing strategy of the individual decsion nodes are also described in decision tables and are often placed higher in the hypothesis inheritance hierarchy for the
purpose of reusing them in different predefined hypothesis. These decision tables are described in functions of the hypothesis classes and are identified with XXXX_Info() and the end of the function name.
The result of such a function is a DN_Info object.
Each hypothesis class also implements a specific decision table to derive the relevant endpoint qualifiers per tier level. (function EndpointQualifiers()). These are used to populate the data matrices and similarity/compare matrices.

Attributes

name	type	domain	inference	comment
`outcome`	:: `HypothesisOutcome`			
`'regulatory info'`	: `String`			
`'targeted testing info'`	: `Strings`			
`'safe-by-design info'`	: `String`			
`'precautionary info'`	: `String`			
`'missing info'`	: `String`			
`consequences`	: `Strings`			
`group`	:: `GroupDescriptor`			

Defined expressions

name	type	expression	comment
title	: String	"A hypothesis"	*The title of the hypothesis.*
lead	: String	"unknown"	*The GRACIOUS partner in lead for this hypothesis.*
description	: String	""	*General description of the hypothesis.*
contributing_scenario	: ContributingScenario	hyp_context.contributing_scenario	*The contributing scenario in case the grouping scenario is based upon a Contributing Scenario. In case the grouping scenario is a direct human or environmental one, the contributing scenario is nil.*
contributing_activity	: ContributingActivity	contributing_scenario→**If**(cs | cs.contributing_activity, **nil**)	*The corresponding contributing activity of the contributing scenario in case one exists, otherwise the value is nil.*
cand_NF	: Nanoform	hyp_context.candidate_scenario.candidate	*This represents the candidate NF to be grouped and selected from the list of provisional nanoforms. It's not necesseraly the same as the target nanoform, it might differ because a release NF, or surrogate NF actually targeted within the hypothesis.*
targ_matr	: Material	hyp_context.material	*The target material is the material under consideration within all hypotheses of this hypotheses context. Mostly it will be the same as the target nanoform, but it can also be ionic/moluecular forms.*
targ_NF	: Nanoform	hyp_context.material **as** Nanoform	*The target NF is the actual NF considered within the hypothesis, it might be the same as the candidate nf, but also a trans-formed or surrogate (e.g. one without a coating etc..)*
targ_medium	: EnvMedium	hyp_context.medium	*This is the targeted medium for the hypotheses within this context.*
NFs_organic_coatings	: Chemicals	targ_NF→**If**(nf | nf.organic_coatings, Chemicals{})	
bio_compartment	: BioCompartment	hyp_context.contributing_scenario→**If**(c | c.receptor, **nil**)	*The biocompartment is derived from the selected contributing exposure scenario.*
env_compartment	: EnvCompartment	hyp_context.env_compartment	
exposure_scenario	: ExposureScenario	hyp_context.contributing_scenario→**If**(c | c.exposure_scenario, **nil**)	
medium_interaction	: medium_interaction	hyp_context.GetInMedium()	
use	: Use	contributing_activity→**If**(ca | ca.use, **nil**)	
NFs_appearance	:: NF_UseForm	use→**If**(u | u.NF_useForm(targ_NF), **nil**)	
aquatic_medium	: AquaticMedium	targ_medium **as** AquaticMedium	
likely_exposure_routes	: ExposureRoutesSet	hyp_context.expected_routes	
hypothesis_context	: HypothesesContext	hyp_context	
scenario_type	:: ScenarioType	hyp_context.scenario_**type**	
tiered	: Boolean	True	
speciation	: Materials	hyp_context.speciation	*These are all materials present in the medium (currently not necessarly at the same time). Needs adaptions...*
sediment_medium	: SedimentMedium	targ_medium **as** SedimentMedium	
soil_medium	: SoilMedium	targ_medium **as** SoilMedium	
purpose	:: GroupingPurpose	hypothesis_context.scenario.purpose	
rationale	: String	""	

Operators

```
function Hypothesis.DeriveOutcome(): HypothesisOutcome
  begin
    /* abstract, to be implemented for each of the derived hypothesis, by default the outcome is not yet implemented */  ;
    result := NYI;
    outcome := NYI;
    group := nil
  end
```

```
function Hypothesis.DetermineOutcome(): HypothesisOutcome
  begin
    /* Initialize / reset of current data.. */  ;
    Reset(group);
    Reset(consequences);
    Reset('missing info');
    Reset('targeted testing info');
    result := DeriveOutcome()
  end


procedure Hypothesis.CSW_ReadAcross_ToChemical()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Read Across: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coChemicalReadAcross
    end;
    with hyp_context | target_context then
      with context_switch | read_across_context then
      begin
        read_across_context.external_medium := target_context.external_medium
      end
  end


procedure Hypothesis.CSW_ReadAcross_ToUncoatedNF()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Read Across: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coUncoatedReadAcross
    end;
    with hyp_context | target_context then
      with context_switch | read_across_context then
      begin
        read_across_context.external_medium := target_context.external_medium
      end
  end


procedure Hypothesis.CSW_Transform_ToNewNF()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Transform: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coTransformationProcess
    end;
    with hyp_context | target_context then
      with context_switch | transformation_context then
      begin
        transformation_context.external_medium := target_context.external_medium
      end
  end
```

```
procedure Hypothesis.CSW_Settle_ToSediment()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Sedimentation: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coSettleProcess
    end;
    with hyp_context | target_context then
      with context_switch | transformation_context then
      begin
        transformation_context.material := target_context.material;
        /* transformation_context.external_medium := Sediment... */
      end
  end

procedure Hypothesis.CSW_Dissolution()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Dissolve: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coDissolutionProcess
    end;
    with hyp_context | target_context then
      with context_switch | read_across_context then
      begin
        read_across_context.external_medium := target_context.external_medium
      end
  end
```

```
procedure Hypothesis.CSW_Transport()
  with hyp_context.SwitchContext() | context_switch then
  begin
    context_switch.name ?= "Transport: ";
    with switch_cause→New | rel then
    begin
      rel.initiating_hypotheses := self;
      rel.switch_contexts := context_switch;
      rel.action := coTransportProcess
    end;
    with hyp_context | target_context then
      with context_switch | transformation_context then
      begin
        transformation_context.material := target_context.material;
        /* transformation_context.external_medium := Sediment... */
      end
  end

function Hypothesis::EndpointQualifiers( tl :: TierLevel ):: EPQs
  /* To be overridden at the lower level. */

function Hypothesis.SourceMaterials(): Materials
  with hyp_context.candidate_scenario | this_cs then
    with this_cs.grouping_scenario | gs then
    begin
      with gs.candidate_scenarios→Excluding(this_cs) | other_css then
      begin
        result := other_css.candidate
      end
    end
```

Class `ExpRelHypothesis` is kind of `Hypothesis`

Well defined hypothesis classes on Exposure and Release

Defined expressions

name	type	expression	comment
tiered	: Boolean	False	

Operators

`function` ExpRelHypothesis.AlwaysEnclosed(): HypothesisOutcome

C1	contributing_scenario | cs	nil	ELSE						
C2	cs.enclosed_activity	-	?	Yes				No	ELSE
C3	cs.open_during_handling	-	-	?	Yes	No	ELSE	-	-
A1	result	IRR	MI	MI	EXCL	INCL	MI	EXCL	MI
		R1	R2	R3	R4	R5	R6	R7	R8

Class `'OC-R'` is kind of `ExpRelHypothesis`

Well defined hypothesis on release in an occupational setting

Class `'OC-R-IND-1'` is kind of `'OC-R'`

Release potential of handling liquid suspensions (spraying of disinfectant and cleaning products, coatings, lubricants, transferring liquids, open baths, spills)

Defined expressions

name	type	expression	comment
title	: String	"OC-R-Ind 1"	
lead	: String	"NRCWE Ana Sofia"	
description	: String	"Release potential of handling liquid suspensions (spraying of disinfectant and cleaning products, coatings, lubricants, transferring liquids, open baths, spills)"	
rationale	: String	"The overarching objective of the hypotheses linked to the release potential of NF into air by using products (e.g. sprays of disinfectant and cleaning products, coatings, and lubricants) is to establish a link between the activity in occupational setting (experimental conditions), and the type of NF used in the liquid suspension. Here the main exposed population are workers and consumers mostly through the inhalation and dermal routes (worst case as oral)."	

Operators

function 'OC-R-IND-1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True																														False
C2	contributing_scenario | cs	nil	ELSE																													-
C3	targ_NF	-	nil	ELSE																												-
C4	cs.ca_perspective	-	-	nil	occupational																										ELSE	-
C5	NFs_appearance	-	-	-	in_suspension																									ELSE	-	-
C6	cs.ca_category	-	-	-	nil	AC_SURFACE_SPRAYING_LIQUIDS, AC_SPRAYING_LIQUIDS_IN_SPACE,AC_APPLICATION_LIQUIDS_HIGH_SPEED_PROCESSES																							ELSE	-	-	-
C7	cs.ca_energy_level	-	-	-	-	nil	el_very_high, el_high						el_medium						el_low,el_very_low, el_none									ELSE	-	-	-	-
C8	cs.used_material.constituents→Exists(c | c.category = 'organic compound')	-	-	-	-	-	True			False			True			False			True			False						-	-	-	-	-
C9	cs.used_material.viscosity | v	-	-	-	-	-	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	ELSE	?	v < 1.0·mPa·s	EXCL	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	INCL	INCL	MI	INCL	INCL	MI	INCL	INCL	MI	INCL	INCL	MI	INCL	INCL	MI	INCL	INCL	MI	INCL	EXCL	MI	IRR	IRR	IRR	IRR
A2	consequences→Add(#)							"Group in level 4: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 3: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"		"Group in level 3: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 2: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"		"Group in level 3: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 2: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"		"Group in level 2: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 1: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"		"Group in level 2: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 1: likely release of NF in droplets See Oc-R-indoor-1e,f,g"		"Group in level 1: likely re-lease of NF in droplets See Oc-R-indoor-1e,f,g"	"Group in level 0: Unlikely release of NF See Oc-R-indoor-1e,f,g"					
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24	R25	R26	R27	R28

Class 'OC-R-IND-2' is kind of 'OC-R'

Mechanical treatment

Defined expressions

name	type	expression	comment
title	: String	"OC-R-Ind 2"	
lead	: String	"ETH Tobias, Jing"	
description	: String	"Release potential of mechanical treatment of NF from a NEP (dependence on the type of NEP matrix, the type of NF and the experimental conditions)"	
rationale	: String	"The overarching objective of the hypotheses linked to the release potential of NF into air (e.g. indoor air) is to establish a link between the activity in occupational setting (experimental conditions), the type of NF and the matrix of a NEP Mechanical treatment (e.g. sanding, abrasion, drilling, grinding, cutting, sawing, shredding, etc) applies a mechanical force to the NM/matrix that can lead to particle release. This release might be affected by the type of matrix, NM incorporated, dispersed, and bonded to the surface of the matrix, and operational conditions (e.g. degradation mechanism). NFs are released into the air in form of NF fragments, NFs embedded or associated with the matrix material throughout the abrasion process. The pristine NF and the matrix define the fraction and concentration of the released and inhalable NF generated during abrasion of NEPs."	

Operators

function 'OC-R-IND-2'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True										False
C2	contributing_scenario | cs	nil	ELSE									-
C3	targ_NF	-	nil	ELSE								-
C4	cs.ca_perspective	-	-	nil	occupational						ELSE	-
C5	NFs_appearance	-	-	-	in_solid_matrix,bound_to_surface					ELSE	-	-
C6	cs.ca_category	-	-	-	nil	AC_IMPACTION_DRY_CONTAMINATED_OBJECTS,AC_FRACTURING_ABRASION_SOLID_OBJECTS			ELSE	-	-	-
C7	cs.used_material | m	-	-	-	-	nil	ELSE		-	-	-	-
C8	m.abrasive_wear_factor | awf	-	-	-	-	-	?	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	NYI	IRR	IRR	IRR	IRR
A2	/* TO BE FURTHER DEVELOPED */							X				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11

Class 'OC-R-IND-3' is kind of 'OC-R'

Release potential of powder handling activities

Defined expressions

name	type	expression	comment
title	: String	"OC-R-Ind 3"	
lead	: String	"NRCWE Ana Sofia"	
description	: String	"Release potential of powder handling activities "	
rationale	: String	"The overarching objective of the hypotheses linked to the release potential of NF into air by handling powders is to establish a link between the activity in occupational setting (experimental conditions), and the type of NF used in a specific activity. Here the main exposed population are workers mostly through the inhalation. Dermal exposure is likely to arise from contact with contaminated surfaces, which can occur through deposition of fugitive emissions. NFs which become airborne in form of pristine-free or aggregated/agglomerated depend mostly on specific activity related factors (type and intensity of the energy applied, duration, amount of material and level of containment) but also on the agglomeration of the bulk material and the level of deagglomeration during release which is also influenced by the relative humidity and temperature of the workplace environment."	

Operators

function 'OC-R-IND-3'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True													False
C2	contributing_scenario | cs	nil	ELSE												-
C3	targ_NF	-	nil	ELSE											-
C4	cs.ca_perspective	-	-	nil	occupational									ELSE	-
C5	NFs_appearance	-	-	-	as_powder								ELSE	-	-
C6	AlwaysEnclosed() | enclosed_outcome	-	-	-	INCL	EXCL				MI	IRR	-	-	-	
C7	cs.ca_energy_level	-	-	-	-	el_very_high, el_high	el_medium	el_low,el_very_low, el_none	ELSE	-	-	-	-	-	
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	EXCL	INCL	INCL	INCL	MI	MI	IRR	IRR	IRR	IRR	
A2	consequences→Add(#)				"Unlikely release of NF."	"Likely release of NF in the form of agglomerates and single particles."	"Likely release of NF in the form of agglomerates and single particles."	"Likely release of NF in the form of agglomerates and single particles."							
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	

Class 'OC-R-IND-4' is kind of 'OC-R'

Well defined hypothesis on release in an occupational setting

Defined expressions

name	type	expression	comment
title	: String	"OC-R-Ind 4"	
description	: String	"Hypothesis related to the release potential of handling liquid suspensions (e.g. transferring, open baths, spills, manual greasing, and lubrication)"	
rationale	: String	"The overarching objective of the hypotheses linked to the release potential of NF into air by handling liquid suspensions with NFs (colloidal suspensions of usually metals, oxides, carbides in fluids with high heat transfer efficiencies) is to establish a link between the activity in occupational setting (experimental conditions), and the type of NF used in a specific activity. Here the main exposed population are workers mostly through the inhalation. Dermal exposure is likely to arise from contact with contaminated surfaces, which can occur through deposition of fugitive emissions. NFs suspended in liquids can become airborne when aerosol mist formation occurs. This generation of mist depends mostly on the viscosity of the liquid and the weight fraction of the substance of interest in the liquid (van Tongeren et al. 2011)."	

Operators

function 'OC-R-IND-4'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True											False
C2	contributing_scenario | cs	nil	ELSE										-
C3	targ_NF	-	nil	ELSE									-
C4	cs.ca_perspective	-	-	nil	occupational							ELSE	-
C5	NFs_appearance	-	-	-	in_suspension						ELSE	-	-
C6	cs.ca_category	-	-	-	nil	AC_ACTIVITY_UNDISTURBED_LIQUID_SURFACE,AC_ACTIVITY_AGITATED_LIQUID_SURFACE,AC_SPREADING_OF_LIQUIDS, AC_FALLING_LIQUIDS, AC_BOTTOM_LOADING_LIQUIDS				ELSE	-	-	-
C7	cs.used_material | m	-	-	-	-	nil	ELSE				-	-	-	-
C8	m.viscosity | v	-	-	-	-	-	?	v < 1.0·mPa·s		ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	MI	MI			IRR	IRR	IRR	IRR	IRR
		R1	R2	R3	R4	R5	R6	R7		R8	R9	R10	R11	R12

Class 'OC-R-OUTD-1' is kind of 'OC-R'

Well defined hypothesis on release in an occupational setting

Defined expressions

name	type	expression	comment
title	: String	"OC-R-Outd 1"	
description	: String	"NF transformation through incineration"	

Operators

function 'OC-R-OUTD-1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True												False
C2	contributing_scenario | cs	nil	ELSE											-
C3	targ_NF	-	nil	ELSE										-
C4	cs.ca_perspective	-	-	nil	occupational								ELSE	-
C5	NFs_appearance	-	-	-	in_suspension			as_powder,in_solid_matrix,bound_to_surface				ELSE	-	-
C6	cs.ca_category	-	-	-	nil	AC_BURNING_OF_LIQUIDS	ELSE	nil	AC_BURNING_OF_SOLIDS	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	NYI	IRR	MI	NYI	IRR	IRR	IRR	IRR	IRR
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	

Class 'OC-HH' is kind of ExpRelHypothesis

Occupational exposure hypothesis (WP2) (Old hypothesis)

Defined expressions

name	type	expression	comment
tiered	: Boolean	False	

Class 'EXP-OCC-D' is kind of 'OC-HH'

Occupational exposure hypothesis

Operators

```
function 'EXP-OCC-D'.DeriveOutcome(): HypothesisOutcome [specialization]
  begin
    outcome := IRR;
    result := outcome
  end
```

Class 'EXP-OCC-O' is kind of 'OC-HH'

Occupational exposure hypothesis

Operators

```
function 'EXP-OCC-O'.DeriveOutcome(): HypothesisOutcome [specialization]
```

C1		-

A1	begin
	  outcome := #;
	  result := outcome
	end
		IRR

		R1

Class 'EXP-OCC-I-D' is kind of 'OC-HH'

Occupational exposure hypothesis

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis EXP-OCC-I-D"	
lead	: String	"IOM?"	
description	: String	"Likelihood of inhalation and dermal exposure in occupational settings"	

Operators

function 'EXP-OCC-I-D'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	False	True																														False
C2	hyp_context.is_start_context	True																													False	
C3	contributing_scenario | cs	nil	ELSE																												-	
C4	targ_NF	-	nil	ELSE																												-	
C5	use.life_cycle_stage	-	-	?	LCS_M,LCS_F,LCS_IS,LCS_PW																										ELSE	-	
C6	cs.ca_perspective	-	-	-	nil	occupational																									ELSE	-	-	
C7	AlwaysEnclosed() | enclosed_outcome	-	-	-	-	INCL	EXCL																						MI	IRR	-	-	-	
C8	NFs_appearance	-	-	-	-	-	in_suspension							as_powder											in_solid_matrix, bound_to_surface				ELSE	-	-	-	-	-	
C9	cs.ca_category	-	-	-	-	-	nil	AC_SURFACE_SPRAYING_LIQUIDS, AC_SPRAYING_LIQUIDS_IN_SPACE	AC_ACTIVITY_UNDISTURBED_LIQUID_SURFACE,AC_ACTIVITY_AGITATED_LIQUID_SURFACE,AC_SPREADING_OF_LIQUIDS,AC_APPLICATION_LIQUIDS_HIGH_SPEED_PROCESSES, AC_FALLING_LIQUIDS, AC_BOTTOM_LOADING_LIQUIDS		ELSE	nil	AC_SYNTHESIS, AC_MOVEMENT_AGITATION_POWDERS_GRANULES,AC_FALLING_POWDERS_GRANULES, AC_VACUUM_TRANSFER_POWDERS_GRANULES,AC_COMPRESSING_POWDERS_GRANULES, AC_SPRAY_APPLICATION_POWDERS		ELSE	AC_IMPACTION_DRY_CONTAMINATED_OBJECTS,AC_FRACTURING_ABRASION_SOLID_OBJECTS		ELSE	-	-	-	-	-	-	
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	EXCL	MI	INCL	INCL		EXCL	MI	INCL		EXCL	INCL		EXCL	EXCL	MI	IRR	IRR	IRR	IRR		IRR
A2	cs.Add_LikelyExposureRoute(inhalation)							X	X				X			X										
A3	cs.Add_LikelyExposureRoute(dermal)							X	X				X			X										
		R1	R2	R3	R4	R5	R6	R7	R8		R9	R10	R11		R12	R13		R14	R15	R16	R17	R18	R19	R20		R21

Class 'ENV-RELEASE' is kind of ExpRelHypothesis

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate

Defined expressions

name	type	expression	comment
title	: String	"Environmental release likely"	
description	: String	"Indicate the compartment the candidate NF is expected to be released into."	

Operators

function 'ENV-RELEASE'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment	ELSE
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR
		R1	R2

Class 'OC-HE-I' is kind of ExpRelHypothesis

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate

Class 'OC-HE-I-1' is kind of 'OC-HE-I'

Likelihood of exposure in occupational processes/activities
(FROM RELEASE TO inhalation EXPOSURE during powder handling, handling of liquid suspension, or mechanical treatment of NEPs – IATA triggered when release is LIKELY)

Defined expressions

name	type	expression	comment
title	: String	"OC-HE-I-1"	
lead	: String	"IOM Araceli"	
description	: String	"Likelihood of exposure in occupational processes/activities (FROM RELEASE TO inhalation EXPOSURE during powder handling, handling of liquid suspension, or mechanical treatment of NEPs - IATA triggered when release is LIKELY)"	

Operators

function 'OC-HE-I-1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True																													False
C2	Hypotheses{Hyp('OC-R-IND-1'), Hyp('OC-R-IND-2'), Hyp('OC-R-IND-3')}.outcome | outcomes	INCL																												ELSE	-
C3	contributing_scenario | cs	nil	ELSE																											-	-
C4	cs.emission_source_segregated_from_receptor	-	?	Yes	No																									-	-
C5	cs.enclosed_activity	-	-	-	?	Yes																			No					-	-
C6	cs.closed_when_NF_is_inside	-	-	-	-	?	Yes								No									-					-	-
C7	cs.localized_extraction_ventilation_used	-	-	-	-	-	?	Yes					No			?	Yes				No			?	Yes				No		-	-
C8	cs.respiratory_protection_equipment_used	-	-	-	-	-	-	?	Yes	No	?	Yes	No	-	?	Yes	No	?	Yes	No	-	?	Yes	No	?	Yes	No	?	Yes	No	-	-
A1	begin outcome := #; result := outcome end	IRR	MI	EXCL	MI	MI	MI	MI	EXCL	EXCL	MI	EXCL	NYI	MI	MI	EXCL	INCL	MI	EXCL	INCL	MI	MI	EXCL	INCL	MI	EXCL	INCL	IRR	IRR		
A2	consequences→Add(#)			"Inhalation & dermal exposure are UNLIKELY"					"Inhalation exposure is UNLIKELY "	"Inhalation exposure is UNLIKELY assuming high protection efficiency of LEV"		"Inhalation exposure is UNLIKELY assuming high protection efficiency of RPE "	"??"			"Inhalation exposure is UNLIKELY assuming high protection efficiency of LEV and/or RPE "	"Inhalation exposure is LIKELY but low assuming high efficiency of LEV "		"Inhalation exposure is UNLIKELY if RPE has a high protection efficiency "	"Inhalation exposure is LIKELY"			"Inhalation exposure is UNLIKELY assuming high protection efficiency of LEV and RPE "	"Inhalation exposure is LIKELY but low assuming a high LEV efficiency "		"Inhalation exposure is UNLIKELY assuming a high protection efficiency"	"Inhalation exposure is LIKELY"		
A3	cs.Add_LikelyExposureRoute(inhalation)																X			X				X			X				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24	R25	R26	R27	R28		

Class 'OC-HE-I-2' is kind of 'OC-HE-I'

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate

Defined expressions

name	type	expression	comment
title	: String	"OC-HE-I-2"	
lead	: String	"IOM Araceli"	
description	: String	"Form of NF during exposure (agglomeration with background particles and removal by gravitational settling)"	

Operators

function 'OC-HE-I-2'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True								False
C2	Hyp('OC-HE-I-1').outcome	INCL							ELSE	-
C3	cand_NF	nil	ELSE						-	-
C4	cand_NF.DN_HARNs_are_rigid_and_needle_like	-	?	Yes	No				-	-
C5	env_compartment as IndoorAir | room	-	-	-	nil	ELSE			-	-
C6	room.background_particle_conc | bc	-	-	-	-	?	bc > 1000000.0·cm⁻³	ELSE	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	MI	INCL	MI	MI	NYI	NYI	IRR	IRR

A2	consequences→Add(#)			"Exposure to PRISTINE FREE NF is LIKELY "						
		R1	R2	R3	R4	R5	R6	R7	R8	R9

Class 'OC-HE-I-3' is kind of 'OC-HE-I'

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate

Defined expressions

name	type	expression	comment
title	: String	"OC-HE-I-3"	

Operators

function 'OC-HE-I-3'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True					False
C2	contributing_scenario | cs	nil	ELSE				-
C3	targ_NF	-	nil	ELSE			-
C4	cs.ca_perspective	-	-	nil	occupational	ELSE	-
C5	NFs_appearance	-	-	-	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	MI	NYI	IRR	IRR

		R1	R2	R3	R4	R5	R6

Class 'OC-HE-I-4' is kind of 'OC-HE-I'

Well defined hypothesis classes on Exposure|Release Human Health and Environmental fate

Defined expressions

name	type	expression	comment
title	: String	"OC-HE-I-4"	
description	: String	"Release potential & exposure likelihood from nanocomposites subject to mechanical treatment (sanding, abrasion, drilling, grinding, cutting, sawing, shredding)"	

Operators

function 'OC-HE-I-4'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	hyp_context.is_start_context	True								False
C2	contributing_scenario | cs	nil	ELSE							-
C3	cs.ca_perspective	-	nil	occupational					ELSE	-
C4	targ_NF	-	-	nil	ELSE				-	-
C5	NFs_appearance	-	-	-	nil	in_solid_matrix		ELSE	-	-
C6	cs.ca_category	-	-	-	-	AC_FRACTURING_ABRASION_SOLID_OBJECTS	ELSE	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	NYI	IRR	IRR	IRR	IRR
		R1	R2	R3	R4	R5	R6	R7	R8	R9

Class HumanHypothesis is kind of Hypothesis

Well defined hypothesis classes on Human Health

Class 'H-I' is kind of HumanHypothesis

Well defined human inhalation hypothesis classes.

Operators

```
function 'H-I'::DN_HARNs_CanDeposit_Info( tl :: TierLevel ) :: DN_Info
```

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→New	X	X	X	X
A2	result.intro	"Estimation of aerodynamic diameter (Dae) from NF size measurements by TEM/SEM NF density measurement"	"Measurement of MMAD by cascade impactor from an airborne dispersion of the material"	"Quantification of lung burden after in vivo inhalation studies."	
A3	result.preferred_methods	"SEM, TEM, STEM (ISO 17200:2020 ISO/TS 80004-6:2015 3.5.5, 3.5.6, 3.5.7 NanoDefine Manual)"	"Cascade Impactor Measurement (ISO/TR 12885:2018(E) C.3.1 C.4.2), Multiple Particle Path Deposition Model (MPPD v3.04 RIVM)"	"STIS, OECD TG412/413"	
A4	result.guidance_for_assay_selection	"Median diameter of constituent particles will be available from the Basic Information. Choice between TEM/SEM/STEM may depend on material type and resolution required for visualization, see NanoDefine manual for guidance. Technical capabilities of user may also need to be considered. Need advice on methods to measure NF density. ISO/TR 12885:2018(E) C.3.1 C.4.2"	"Multiple Path Particle Deposition model is a well characterised approach for estimation of deposition of spherical particles after inhalation. Alternative models which may be more appropriate for high aspect ratio NFs may be available and should be considered."	"Quantification of lung burden is now included in the updated OECD TG 412/413 for 28-Day and 90-Day Inhalation Toxicity Studies and required at exposure termination (PEO-1) and therefore should also be included in STIS studies. Additional guidance in the design of the inhalation studies is provided in OECD GD39. Alternative in vivo models such as intratracheal instillation which are not physiologically relevant are not suitable to address this decision node. "	
A5	result.tier_escalation	"For homogenous HARN samples composed of single straight fibres Tier 1 is sufficient to make prediction of likelihood of deposition into the distal regions of the lung upon inhalation exposure with high level of confidence from estimated Dae. For more heterogenous HARN Dae should be confirmed at Tier 2."	"Models of lung deposition have largely been developed based on spherical particles as such modelling deposition pattern of fibrous material have a high level of associated uncertainty due to the complexity. Quantitative similarity assessment of predicted pattens of deposition can provide evidence to justify read-across to allow waiving of inhalation studies dependent on the level of similarity, quality of data and degree of uncertainty in the results. "		
A6	/* Transmission Electron Microscopy */	X			
A7	result.epqs→Add(WTG(PER(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Sterile filtered water'), 50.0·%)))	X			
A8	/* Helium pycnometry */	X			
A9	result.epqs→Add(WTG(EPQ(PC_DENSITY::EP_SKELETAL_DENSITY)))	X	X	X	
A10	/* Cascade Impactor Measurement */				
A11	result.epqs→Add(WTG(EPQ(PC_GRANULOMETRY::EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER)))		X		
A12	result.epqs→Add(WTG(EPQ(PC_GRANULOMETRY::EP_AERODYNAMIC_EQ_SPHERE_DIAMETER)))		X		
A13	/* Multiple Path Particle Dosimetry model */				
A14	result.epqs→Add(WTG(EPQ(HH_LUNG_DEPOSITION::EP_DEPOSITION_FRACTION_TRACHEA_BRONCHI)))		X		
A15	result.epqs→Add(WTG(EPQ(HH_LUNG_DEPOSITION::EP_DEPOSITION_FRACTION_ALVEOLI)))		X		
A16	/* In vivo lung burden studies... endpoints are currently missing.. TO DO VNR */				
A17	result.epqs→Add(WTG(EPQ(HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx)))			X	
		R1	R2	R3	R4

function 'H-I'::DN_Dissolution_LSF_Info(tl :: TierLevel):: DN_Info

C1	tl	-
A1	result := DN_Info→**New**	X
A2	result.intro	"Acellular dissolution measurements."
A3	result.preferred_methods	"Dynamic dissolution in lung lining fluid (pH 7.4) (ISO/TR 19057:2017)"
A4	result.guidance_for_assay_selection	"According to ISO19057 repeat measurements from a static dissolution system can be conducted over time to allow dissolution rate to be calculated. Measurement of dissolution by continuous flow system is based on elemental analysis of solute, method not appropriate for carbonaceous material. Method recommended for other materials which can be detected by elemental analysis as continuous flow avoids system reaching an equilibrium which may restrict dissolution. ISO19057:The dissolution method is a standardized assay that describes the use of both static and dynamic systems. However, testing NF dissolution in a dynamic condition is considered the preferred method as the results are consistent with data from in vivo studies (NanoImpact 12 (2018) 29-41)"
A5	/* Static dissolution test */	
A6	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, 'Simulated lung airway lining fluid')))	X
A7	/* Continuous Flow System */	
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated lung airway lining fluid')))	X
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated lung airway lining fluid')))	X
		R1

function 'H-I'::DN_HARN_Dissolution_LSF_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Screening batch dissolution or continuous flow test in lung lining fluid (pH 7.4)"	
A3	result.preferred_methods		
A4	result.guidance_for_assay_selection	"Static dissolution system based on gravametric analysis is suitable for carbonaceous material e.g. MWCNT (see Osmond-McLeod 2011 doi: 10.1186/1743-8977-8-15). Not suitable for NF predicted to rapidly dissolve due to saturation of the medium which leads to the inhibition of dissolution when equilibrium is reached. According to ISO19057 repeat measurements from a static dissolution system can be conducted over time to allow dissolution rate to be calculated. Measurement of dissolution by continuous flow system is based on elemental analysis of solute, method not appropriate for carbonaceous material. Method recommended for other materials which can be detected by elemental analysis as continuous flow avoids system reaching an equilibrium which may restrict dissolution."	
A5	result.tier_escalation		
A6	/* Static dissolution test */		
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, 'Simulated lung airway lining fluid')))	X	
A8	/* Continous Flow System */		
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated lung airway lining fluid')))	X	
A10	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated lung airway lining fluid')))	X	
		R1	R2

function 'H-I'::DN_Dissolution_PSF_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Screening batch dissolution or continuous flow test in simulated lung macrophage phagolysosomal fluid (pH 4.5)"	"Cellular dissolution measurements"	"In vivo dissolution measurement"	
A3	result.preferred_methods		"Measuring dissolution in macrophages"	"Measuring lung burden and clearance kinetics after in vivo exposure (short-term inhalation study (STIS), OECD GD39)"	
A4	result.guidance_for_assay_selection	"According to ISO19057 repeat measurements from a static dissolution system can be conducted over time to allow dissolution rate to be calculated. Measurement of dissolution by continuous flow system is based on elemental analysis of solute, method not appropriate for carbonaceous material. Method recommended for other materials which can be detected by elemental analysis as continuous flow avoids system reaching an equilibrium which may restrict dissolution. ISO19057:The dissolution method is a standardized assay that describes the use of both static and dynamic systems. However, testing NF dissolution in a dynamic condition is considered the preferred method as the results are consistent with data from in vivo studies (NanoImpact 12 (2018) 29-41)"	"No protocol has yet been validated for intracellular dissolution studies. Suggested protocol based on Koltermann-Jully et al 2018. Detection, retrieval and quantification of NF post exposure may be material specific."	"Intratracheal instillation is not considered a physiological route of exposure and should only be considered as indicative of NM biopersistence in tissue and not a substitute for inhalation studies for the determination of physiologically-relevant clearance rates or extrapolation to human exposure scenarios for risk assessment. OECD GD39 reviews the limitations of this route of exposure and provides guidance on the appropriate use and interpretation of hazard derived from instillation studies. Inclusion of lung burden measurement at a number of timepoints post inhalation exposure is recommended by OECD GD39 to allow half-life of likely poorly soluble particles to be determined. Additional guidance in the design of the inhalation studies is provided in OECD GD39. Quantification of lung burden is now included in the updated OECD TG 412/413 for 28-Day and 90-Day Inhalation Toxicity Studies recommended to be performed at exposure termination (PEO-1) and at 2 additional PEOs (PEO-2 and PEO-3) to allow half-life of likely poorly soluble particles to be determined. Additional guidance is provided in OECD GD39."	
A5	result.tier_escalation	"Tier 1 assay confirms durability in neutral pH environment to mimic lung lining fluid and low pH environment to mimic the macrophage phagolysome. Progress to Tier 2 To assess durability in more biologically relevant system and confirm resistance to enzymatic/ oxidative degradation. Progression to Tier 2 will dependent on user needs (higher level of confidence in durability outcome) and expert judgement (knowledge on susceptibility of different material types to enzymatic/oxidative degradation may lead to recommendation to move to Tier 2) "	"Progression to Tier 2 is envisioned to be only used in some cases where a more physiologically relevant cellular system is required to better understand mechanism.Increased predictivity over Tier 1 assays for grouping purposes has not been demonstrated. Direct Progression from Tier 1 to Tier 3 to support grouping for regulatory purposes may be more efficient/ cost effective."	"Evidence of biopersistence from Tier 3 in vivo studies supports grouping of NFs as very slowing dissolving for all purposes. Quantitative similarity assessment of clearance rates and/or half-life from instillation or STIS studies can provide evidence to justify read-across to allow waiving of longer-term inhalation studies dependent on the level of similarity, quality of data and degree of uncertainty in the results. "	
A6	/* Static and continuous flow */				
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, 'Simulated lung macrophage phagolysosomal fluid')))	X			X
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated lung macrophage phagolysosomal fluid')))	X			X
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated lung macrophage phagolysosomal fluid')))	X			X
A10	/* Macrophage-assisted dissolution assay */				
A11	result.epqs→Add(WTG(CELL(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_MASS_ LOSS, 'Cell culture medium, pH 7.4'), 'NR8383 (rat alveolar macrophages cell line)')))		X		
A12	result.epqs→Add(WTG(CELL(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_HALF_ **TIME**, 'Cell culture medium, pH 7.4'), 'NR8383 (rat alveolar macrophages cell line)')))		X		
A13	result.epqs→Add(WTG(CELL(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_RATE, 'Cell culture medium, pH 7.4'), 'NR8383 (rat alveolar macrophages cell line')))		X		
A14	/* STIS, Repeated dose 28/90 inhalation study */				
A15	result.epqs→Add(WTG(EPQ(HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx)))			X	
A16	result.epqs→Add(WTG(EPQ(HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_**TIME**)))			X	
A17	result.epqs→Add(WTG(EPQ(HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE)))			X	
A18					
		R1	R2	R3	R4

function 'H-I'::DN_HARN_Dissolution_PSF_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Screening batch dissolution or continuous flow test in phagolysosmal fluid (pH 4.5)"	"Macrophage-assisted dissolution assay"	"Quantification of lung burden and clearance kinetics within in vivo studies inhalation (OECD TG 412/413)"	
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection	"According to ISO19057 repeat measurements from a static dissolution system can be conducted over time to allow dissolution rate to be calculated. Static dissolution system based on gravametric analysis is suitable for carbonaceous material e.g. MWCNT (see Osmond-McLeod 2011 doi: 10.1186/1743-8977-8-15). Not suitable for NF predicted to rapidly dissolve due to saturation of the medium which leads to the inhibition of dissolution when equilibrium is reached Measurement of dissolution by continuous flow system is based on elemental analysis of solute, method not appropriate for carbonaceous material. Method recommended for other materials which can be detected by elemental analysis as continuous flow avoids system reaching an equilibrium which may restrict dissolution."	"No protocol has yet been validated for intracellular dissolution studies. Suggested protocol based on Koltermann-Jully et al 2018. Detection, retrieval and quantification of NF post exposure may be material specific."	"Intratracheal instillation is not considered a physiological route of exposure and should only be considered as indicative of NM biopersistence in tissue and not a substitute for inhalation studies for the determination of physiologically-relevant clearance rates or extrapolation to human exposure scenarios for risk assessment. OECD GD39 reviews the limitations of this route of exposure and provides guidance on the appropriate use and interpretation of hazard derived from instillation studies. Inclusion of lung burden measurement at a number of timepoints post inhalation exposure is recommended by OECD GD39 to allow half-life of likely poorly soluble particles to be determined. Additional guidance in the design of the inhalation studies is provided in OECD GD39. Quantification of lung burden is now included in the updated OECD TG 412/413 for 28-Day and 90-Day Inhalation Toxicity Studies recommended to be performed at exposure termination (PEO-1) and at 2 additional PEOs (PEO-2 and PEO-3) to allow half-life of likely poorly soluble particles to be determined. Additional guidance is provided in OECD GD39."	
A5	result.tier_escalation	"Use of Tier 2 intracellular dissolution assay may provide further mechanistic understanding of NM biodurability and envisioned to be more applicable for targeted testing to increase understanding of hazard potential. Increased predictivity over Tier 1 assays for grouping purposes has not been demonstrated. Direct Progression from Tier 1 to Tier 3 to support grouping for regulatory purposes may be more efficient/ cost effective."	"Evidence of HARN biopersistence from Tier 3 in vivo studies supports grouping of HARN as very slowing dissolving for all purposes. Quantitative similarity assessment of clearance rates and/or half-life from instillation or STIS studies can provide evidence to justify read-across to allow waiving of longer-term inhalation studies dependent on the level of similarity, quality of data and degree of uncertainty in the results."		
A6	/* Batch dissolution test */				
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, 'Simulated lung macrophage phagolysosomal fluid')))	X			
A8	/* Continous Flow System */				
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated lung macrophage phagolysosomal fluid')))	X			
A10	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated lung macrophage phagolysosomal fluid')))	X			
A11	/* Batch dissolution or Continuous Flow System */				
A12	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_TRANSFORMATION_D1, 'Simulated lung macrophage phagolysosomal fluid')))				
A13	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_TRANSFORMATION_D3, 'Simulated lung macrophage phagolysosomal fluid')))				
A14	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_TRANSFORMATION_MORPHOLOGY, 'Simulated lung macrophage phagolysosomal fluid')))				
A15	/* Durability in cellular systems */				
A16	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_MASS_LOSS, 'Cell culture medium, pH 7.4')))		X		
A17	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_RATE, 'Cell culture medium, pH 7.4')))		X		
A18	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_HALF_**TIME**, 'Cell culture medium, pH 7.4')))		X		
A19	/* In vivo intratracheal instillation, In vivo inhalation */				
A20	result.epqs→Add(WTG(EPQU(HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx, ·mg·g^{-1})))			X	
A21	result.epqs→Add(WTG(EPQU(HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_**TIME**, ·d)))			X	
A22	result.epqs→Add(WTG(EPQU(HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE, ·µg·d^{-1})))			X	
		R1	R2	R3	R4

function 'H-I'::DN_FibreLength_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"NF size measurements by TEM/SEM"	"NF size measurements by TEM/SEM from an airborne dispersion of the material"		
A3	result.preferred_methods	"TEM/SEM/STEM"	"TEM/SEM/STEM on aerosolised sample"		
A4	result.guidance_for_assay_selection	"Choice between TEM/SEM/STEM may dependent on material type and resolution required for visualization, see NanoDefine manual for guidance. Technical capabilities of user may also need to be considered. Choice of dispersion media may relate to user needs, dispersion in water will reflect the intrinsic morphology of the HARN, Inclusion of protein (NANOGENOTOX dispersion) or use of cell culture media may be chosen to assess exposure relevant forms aligned to additional DNs or endpoints e.g. to allow morphology to be related to in vitro hazard assessment results. Tier 1 of DN can be at constituent particle level or agglomerate/aggregate level. Choice depends on material under investigation and can be decided by initial qualitative EM assessment of NFs. NB particle size level is not interchangeable at must be the same for each NFs to allow comparison for grouping."	"Choice between TEM/SEM/STEM may dependent on material type and resolution required for visualization, see NanoDefine manual for guidance. Technical capabilities of user may also need to be considered. Tier 2 size distribution data from aerosol may be available or combined with other endpoints e.g. from dustiness assessment "		
A5	result.tier_escalation	"Tier 1 assessment of the size profiles of HARN in suspension does not necessarily reflect the size profile of the HARN when aerosolized. Tier 2 requires the measurement of shape and size profiles from aerosolized samples and will provide confirmation that the HARN in aerosolized form will meet the threshold. Tier 2 provides greater certainty in adherence of exposure-relevant form of HARN to DN criteria."			
A6	/* SEM/TEM/STEM in sterile-filtered-water */				
A7					
A8	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D3, 'Sterile filtered water'), slConstituentParticleLevel)))	X			
A9	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_FERET_DIAMETER_D3, 'Sterile filtered water'), slAgglomerateLevel)))	X			
A10					
A11	/* SEM/TEM/STEM in NANOGENTOX dispersion media */				
A12	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D3, 'NANOGENTOX dispersion media'), slConstituentParticleLevel)))	X			
A13	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_FERET_DIAMETER_D3, 'NANOGENTOX dispersion media'), slAgglomerateLevel)))	X			
A14	/* SEM/TEM/STEM in cell culture media */				
A15	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_FERET_DIAMETER_D3, 'Cell culture media'), slConstituentParticleLevel)))	X			
A16	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D3, 'Cell culture media'), slAgglomerateLevel)))	X			
A17	/* SEM/TEM/STEM on aerosolised sample*/				
A18	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_FERET_DIAMETER_D3, 'Aerolisation medium'), slConstituentParticleLevel)))		X		
A19	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D3, 'Aerolisation medium'), slAgglomerateLevel)))		X		
		R1	R2	R3	R4

function 'H-I'::DN_Rigid_Fibrous_Needles_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Measure diameter of NF by TEM, supporting EM"	"Size measurements of prevalent secondary structure by TEM/SEM."		
A3	result.preferred_methods	"SEM, TEM, STEM"	"SEM, TEM, STEM"		
A4	result.guidance_for_assay_selection	"It is important to note that HARN such as MWCNT have the propensity to form agglomerates which may result in the formation of aligned bundles of HARNs with a fibrous structure. This may include HARN which on an individual fibre basis would be considered non-rigid but when agglomerated together will present a rigid fibre-like structure. As the secondary structure is what cells in the tissue will encounter it should be considered the biologically-relevant form potentially driving hazard. Therefore, a clear distinction between the different structures of the HARN which are under investigation should be made to allow grouping of 'like with like'. Supporting EM images are needed to confirm whether the HARN are present as individual fibres, within aligned fibrous bundles, tangled fibrous agglomerates or granular agglomerates."	"Tier 2 methods addressing HARN rigidity and maintenance of fibrous morphology are based on assessment of an aerosolised sample of the HARN. Tier 2 size distribution data from aerosol may be available or combined with other endpoints e.g. from dustiness assessment."		
A5	result.tier_escalation	"Tier 1 assessment of the size profiles of HARN in suspension does not necessarily reflect the size profile of the HARN when aerosolized. EM images should be used to provide confidence in the appropriateness of grouping for the hypothesised hazard potential on individual fibre basis where radically different secondary structures would suggest an escalation to Tier 2. This assessment is based on both low and high power EM to identify the size of individual fibres and overall state of agglomeration. Tier 2 requires the measurement of shape and size profiles from aerosolized samples and will provide confirmation that the HARN in aerosolized form will meet the threshold."	"No higher tier required."		
A6	/* SEM, TEM, STEM in sterile-filtered water */				
A7	result.epqs→Add(WTG(MED(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASSEMBLY_STRUCTURE_AGG), 'Sterile filtered water')))	X			
A8	result.epqs→Add(WTG(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slConstituentParticleLevel), 'Sterile filtered water')))	X			
A9	result.epqs→Add(WTG(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slAgglomerateLevel), 'Sterile filtered water')))	X			
A10	result.epqs→Add(WTG(MED(ENUM(EPQ(EP_ASPECT_RATIO_D3_D1), slAgglomerateLevel), 'Sterile filtered water')))	X			
A11	/* SEM, TEM, STEM using aerosiolised sample*/				
A12	result.epqs→Add(WTG(MED(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASSEMBLY_STRUCTURE_AGG), 'Aerolisation medium')))		X		
A13	result.epqs→Add(WTG(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slConstituentParticleLevel), 'Aerolisation medium')))		X		
A14	result.epqs→Add(WTG(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slAgglomerateLevel), 'Aerolisation medium')))		X		
A15	result.epqs→Add(WTG(MED(ENUM(EPQ(EP_ASPECT_RATIO_D3_D1), slAgglomerateLevel), 'Aerolisation medium')))		X		
		R1	R2	R3	R4

function 'H-I'::DN_Frustrated_Phagosytosis_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Inflammasome activation"	"In vitro granuloma formation"		
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection	"A panel of quantitative and qualitative endpoints indicative of frustrated phagocytosis should be assessed to address this DN (see Murphy et al 2021 for justification of selection of endpoint panel) and include both biochemical read-outs as well as supporting microscopy images. Exposure Dose range tested should be based on sublethal dose range determined from dose range finding study. Dosimetry needs to be carefully considered and evidenced. Potential for HARN interference in detecting assay endpoints should be tested and discounted."	"Assay not validated, should only be used for targetted testing to further illuminate potential similarity in terms on MoA. Phenotypic analysis of the granuloma may provide more information regarding the similarity of HARN MoA or reduce the uncertainty about divergent of MoA, i.e. IL-1b release not related to fibre morphology.."		
A5	result.tier_escalation	"Tier 1 indicates acute activation of the NALP3 inflammasome via the disruption of the lysosome resulting in the release of the pro-inflammatory cytokine, IL-1β. Tier 2 indicates a chronic pro-inflammatory outcome due to frustrated phagocytosis. Progression to Tier 2 triggered by the user need for further mechanistic information on the potential for the NF to cause a chronic response. Tier 2 information can be used to strenghten a similarity assessment to support read-across. Lysosomaldamage in this system is not related to high surface area or sharp nanoscale surface features, but rather to length and stiffness."	"Tier 2 can support Tier 1 assessment of similarity and provide insight into MoA. However, model is novel and has not been tested/used extensively therefore if conditions are met then progression to next DN is supported however if conditions are not met then default to Tier 1 rather than exit the IATA."		
A6	/* Inflammasome activiation, PATROLS, NANOREFINE SOP */				
A7	result.epqs→Add(WTD(CELL(ENUM(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), BM_CYTOKINES::'IL-1B'), 'THP-1 (human leukemic monocyte cell line)')))	X			
A8	result.epqs→Add(WTD(CELL(ENUM(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), BM_CYTOKINES::'IL-18'), 'THP-1 (human leukemic monocyte cell line)')))	X			
A9	result.epqs→Add(WTD(EPQ(HH_INFLAMMATION::EP_CATHEPSINB_RELEASE)))	X			
A10	result.epqs→Add(WTD(EPQ(HH_INFLAMMATION::EP_LYSOSOMAL_DISRUPTION)))	X			
A11	/* In vitro granuloma formation, Development of 3D granuloma in response to long-term in vitro exposure to NF based on model from Sanchez et al 2011. */		X		
A12	result.epqs→Add(WTD(EPQ(HH_INFLAMMATION::EP_IN_VITRO_GRANULOMA_FORMATION)))		X		
		R1	R2	R3	R4

function 'H-I'::DG_HARN_Inflammation_Info(tl :: TierLevel) :: DN_Info

C1	tl	-
A1	/* H-I-1, H-I-2 */	
A2	/* Fiona, to confirm same TTS as for non HARN ?*/	
A3	result := DG_Inflammation_Info(tl)	X
		R1

function 'H-I'::DG_HARN_Genotoxicity_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-I-1, H-I-2 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Genotoxicity (TO DO)"	"Genotoxicity (TO DO)"	"Genotoxicity (TO DO)"	
		R1	R2	R3	R4

function 'H-I'::DG_Reactivity_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3
A1	/* H-I-Q, H-I-G, H-I-S */			
A2	result := DN_Info→**New**	X	X	X
A3	result.intro	"Acellular ROS measurements."	"Cellular oxidative stress measurement."	"In vivo oxidative stress measurement."
A4	result.preferred_methods	"FRAS, DCFH2-DA, EPR"	"Measuring protein carbonylation (NanoReg2 SOP)"	"Measuring oxidative stress after in vivo exposure (STIS, OECD GD39)"
A5	result.guidance_for_assay_selection	"Different approaches to Tier 1 assessment of surface reactivity may be taken dependent on the purpose of grouping. For example, for SbD purposes where the aim may be to compare similarity of surface reactivity across NFs of different chemical composition or NFs with the same core and a different coating, a combination of assays would be recommended for a broader assessment of reactivity. Conversely, for grouping NFs for regulatory purposes, such as the development of a read-across argument, comparison of surface reactivity of different NFs or non-NFs via a combination of assays might add unnecessary complexity. Therefore, a single assay that is sensitive to the substance-specific reactivity should be selected [75]. Guidance: EPR has the least interference with hydrophobic and colored substances, however, carbonaceous materials can interfere with the assay. The FRAS assay has been demonstrated to be suitable for testing both metal-containing NFs and carbonaceous materials [75]. DCFH2-DA assay is suitable for testing of carbonaceous materials [75]."	"Tier 2 involves cellular assessment of oxidative stress as a biological consequence of NF reactivity. Guidance: Measuring protein carbonylation in cells has been shown to give a similar ranking of NFs compared to adverse reactions (such as inflammation) after short-term in vivo inhalation studies (STIS) [77]. Measuring glutathione depletion showed a correlation between in vitro and in vivo exposure for amorphous silica nanoparticles [78]. The disadvantage of measuring glutathione is that it is easily reduced during sample preparation making it difficult to assess the reduced and the oxidized form. An alternative method could be the use of antioxidants to assess whether specific endpoints (e.g. cytokine production) are oxidant mediated. For NFs that are considered either gradually or quickly dissolving based on their dissolution rate, the relative contribution of the ion and particle components to the toxicity observed during hazard testing will need to be determined [79]. Also the potential for the particle and ion to interact to enhance toxicity should be considered [76]."	"If Tier 3 in vivo studies are required to enable a grouping decision or to facilitate a read-across argument, measuring glutathione depletion and lipid peroxidation after short-term inhalation can be considered. In addition, endpoints such as oxidative DNA damage (by measuring 8-hydroxy-2-deoxyguanosine (8-OHdG)) may be included in the histopathological assessment of tissue to provide evidence of oxidative stress in vivo [39]."
A6	result.tier_escalation	"Current research shows that a range of intrinsic factors like shape, size, coating, composition, crystallinity, impurities [15, 32-34], and extrinsic factors such as pH, temperature, ionic strength and protein binding may modulate the surface reactivity of NFs. Tier 1 provides information on the NF surface reactivity without cells. To increase confidence in the similarity between a target NF and a source material, the user can decide to gather information on the biological reactivity of the NF (Tier 2 assays in cells)."	"Tier 2 assays will provide more information in a more physiologically-relevant context compared to Tier 1 supporting the outcome that the target NF(s) have the same reactivity response compare to a source material. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."	
A7	/* FRAS http://iopscience.iop.org/1742-6596/838/1/012033 */	X		
A8	result.epqs→Add(WTD(EPQM(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE, 'Human blood serum (HBS)')))	X		
A9	result.epqs→Add(WTD(EPQM(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE, 'Human blood serum (HBS)')))	X		
A10	/* DCFH2-DA (SOP in D5.3 of GRACIOUS) */	X		
A11	result.epqs→Add(WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU)))	X		
A12	result.epqs→Add(WTD(OP(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU), oPEAK)))	X		
A13	/* EPR (ISO TS 18827, ISO 2017)*/	X		
A14	result.epqs→Add(WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY)))	X		
A15	/* DCFH2-DA cellular (NanoReg D5.06 SOP Annex 5 using FACS) */		X	
A16	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_RFU_CHANGE)))		X	
A17	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_AIR_LIQUID_INTERFACE_PERC_OF_CONTROL)))		X	
A18	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL)))		X	
A19	/* Protein carbonylation */		X	
A20	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN)))		X	
A21	/* Protein carbonylation in BSA corona */		X	
A22				
A23	/* GSH depletion */		X	
A24	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_CHANGE_IN_GSH_LEVEL)))		X	
A25	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION)))		X	
A26	/* ER stress (stress the endoplasmic reticulum) */		X	
A27				
A28	/* Heat Shock Protein (HSP) activiation, WB?, ELISA, FACS?*/		X	
A29	result.epqs→Add(WTD(EPQ(HH_IMMUNOTOXICITY::EP_HEAT_SHOCK_PROTEIN_PERC_OF_CONTROL)))		X	
		R1	R2	R3

function 'H-I'::DG_Inflammation_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-I-Q, H-I-G, H-I-S */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cellular measurements of inflammation potency using cell lines and submerged exposure."	"Cellular measurements of inflammation potency using advanced physiologically relevant in vitro models."	"In vivo measurement of inflammation potency."	
A4	result.preferred_methods	"Measuring inflammasome activation in THP-1 cells (REFINE SOP)"	"Measuring cytokine production in co-culture models using air-liquid exposure."	"Measuring influx of inflammatory cells and production of cytokines in the bronchoalveolar lavage fluid (BALF) and histological examination of respiratory tract after in vivo exposure (STIS, OECD GD39)"	
A5	result.guidance_for_assay_selection	"The preferred assay measures inflammasome activation in the human monocyte cell-line THP-1 (SOP from REFINE (Vandebriel et al. submitted 2021)). Another suitable Tier 1 in vitro assay that can be used to assess macrophage activation and inflammatory potential of NFs is based on rat alveolar macrophages (NR8383)."	"Therefore, at Tier 2 we recommend using an air-liquid interface (ALI) exposure to mimic inhalation exposure more closely [87]. Another way of enhancing predictivity is to better mimic physiological relevance of the in vitro model by using co-cultures or tissue models cultured from primary cells. SOPs and publications [91] [93] from the H2020 project PATROLS (https://www.patrols-h2020.eu), provide useful information towards improved standardization of these methods. The downside of these more complex models is that these methods have not been validated or standardized and are undergoing constant optimizations to allow better predictions [87]."	"We recommend that if in vivo studies are considered, inclusion of Tier 3 measurements for all DN (dissolution and reactivity) are combined within one study to avoid additional in vivo testing for the other DN. STIS should be performed following recommendation of OECD Guidance Document 39 [95]. Nose-only is the most preferred exposure mode [96]. In case that a study according to OECD test guidelines [73, 74] is required later on for regulatory purposes, the STIS data can assist the scientist to appropriately design their regulatory study."	
A6	result.tier_escalation	"Submerged exposure can greatly alter particle characteristics compared to the airborne state. Therefore, the user could decide to progress to Tier 2 assays and use air-liquid interface (ALI) exposure to mimic inhalation exposure more closely [87]. However, ALI exposure models and more complex lung models have not been validated or standardized and undergo constant optimizations."	"As inflammation is a complex process, Tier 3 short-term inhalation studies (STIS) [94] might be required to substantiate a read-across argument. This depends on expert judgement."		
A7	/* Inflammasome activation, REFINE SOP (Vandebriel et al. 2021), THP-1 human monocytes cell line */				
A8	result.epqs→Add(WTD(CELL(ENUM(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), BM_CYTOKINES::'LDH'), 'THP-1 (human leukemic monocyte cell line)')))	X			
A9	result.epqs→Add(WTD(CELL(ENUM(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), BM_CYTOKINES::'TNF-A'), 'THP-1 (human leukemic monocyte cell line)')))	X			
A10	/* Macrophage differentiation, RIVM SOP, Primary human cells: monocyte-derived macrophages (MDM) */	X			
A11	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'MDM (human primary cells: monocyte-derived macrophages)')))	X			
A12	/* Cytokine release in cell lines, Several cell lines, including A549, Calu-3, THP-1, 16HBE */	X			
A13	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'A549 (human alveolar cell line)')))	X			
A14	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'Calu-3 (human bronchial cell line)')))	X			
A15	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), '16HBE (human bronchial epithelial cell line)')))	X			
A16	/* Cytokine release in co-culture models, PATROLS SOPs, Calu-3 + MDM/dTHP-1, A549 + dTHP-1 */		X		
A17	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'Calu-3 + MDM co-culture')))		X		
A18	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'Calu-3 + dTHP-1 co-culture')))		X		
A19	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'A549 + dTHP-1 co-culture')))		X		
A20	/* Cytokine release in 3D models, EpiAlveolar (MatTek) or MucilAir (Epithelix) or from culturing primary cells into 3D models */		X		
A21	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'EpiAlveolar (human 3D co-culture cell model)')))		X		
A22	result.epqs→Add(WTD(CELL(EPQ(HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE), 'MucilAir (human 3D cell model)')))		X		
A23	/* Cytokine release in air-liquid exposed models, PATROLS SOPs, Calu-3 + MDM/dTHP-1, A549 + dTHP-1 */		X		
A24					
A25	/* Short-term inhalation study protocol (STIS) BALF analysis */			X	
A26					
A27	/* Short-term inhalation study protocol (STIS) Histopathology */			X	
A28	/* 28-Day (Subacute) Inhalation Toxicity Study BALF analysis */			X	
A29	/* 28-Day (Subacute) Inhalation Toxicity Study Histopathology */			X	
A30	/* 90-Day (Subchronic) Inhalation Toxicity Study BALF analysis */			X	
A31	/* 90-Day (Subchronic) Inhalation Toxicity Study Histopathology */			X	
		R1	R2	R3	R4

Class 'H-I-1' is kind of 'H-I'

Hypothesis H-I-1: Respirable, biopersistent, rigid HARN: Following inhalation, long-term pulmonary retention of particles can occur resulting in lung toxicity.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-I-1"	
lead	: String	"HWU (Fiona)"	
description	: String	"Respirable, biopersistent, rigid HARN: Following inhalation, long-term pulmonary retention of particles can occur resulting in lung toxicity."	
rationale	: String	"Grouping of NFs according to the HARN hypothesis may have a number of potential implications including facilitating the generation of a read-across argument for risk assessment which may allow waiving of testing for regulatory purposes (e.g. the completion of a registration dossier) and the to support the adoption of a derived no effect level (DNEL) for materials on which limited hazard data is available. Grouping according to the HARN mesothelioma hypothesis may also be used to guide and support the innovation of SbD materials or fill data gaps and increase scientific understanding of key mechanisms of fibre pathogenicity thereby further streamlining the risk assessment process in the future."	

Operators

function 'H-I-1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman																				ELSE	
C2	targ_NF	nil	ELSE																			-	
C3	likely_exposure_routes	-	0	inhalation																	ELSE	-	
C4	targ_NF.is_HARN	-	-	?	Yes															ELSE	-	-	
C5	targ_NF.DN_HARN_can_deposit_in_distal_region_of_lung	-	-	-	?	Yes													No	-	-	-	
C6	targ_NF.DN_HARNs_dissolve_very_slow_in_lung_lining_fluid	-	-	-	-	?	Yes											ELSE	-	-	-	-	
C7	targ_NF.DN_HARNs_dissolve_very_slow_in_lysosomal_fluid	-	-	-	-	-	?	Yes									ELSE	-	-	-	-	-	
C8	targ_NF.DN_HARN_length_exceeds_5_micron	-	-	-	-	-	-	?	Yes							No	-	-	-	-	-	-	
C9	targ_NF.DN_HARNs_are_rigid_and_needle_like	-	-	-	-	-	-	-	?	Yes					No	ELSE	-	-	-	-	-	-	
C10	targ_NF.DN_HARNs_cause_frustrated_phagocytosis	-	-	-	-	-	-	-	-	?	Yes			No	ELSE	-	-	-	-	-	-	-	
C11	source_material	-	-	-	-	-	-	-	-	-	nil		ELSE	-	-	-	-	-	-	-	-	-	
C12	purpose	-	-	-	-	-	-	-	-	-	'regulatory'	ELSE	-	-	-	-	-	-	-	-	-	-	
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	MI	MI	MI	MI	MI	INCL		INCL	EXCL	MI	EXCL	MI	EXCL	EXCL	EXCL	EXCL	IRR	IRR	IRR
A2	consequences→Add(#)													"Macrophage uptake"		"Macrophage uptake"		"Macrophage uptake"	"Dissolution in lysosomes, breakage and shortening of long fibres."		"Deposition primarly in the upper airways, efficient muco-cilliary clearance."			
A3	consequences→Add(#)										"Regulatory: Read-across to source is not possible."	"Precautionary/ SbD: Assume NF can cause inflammation and fibrosis or cancer."	"Perform read-across to source material for impaired clearance, chronic inflammation and potential tumour formation."	"Consider H-I-S for non-fibrous NFs with very slow dissolution rates."		"Consider H-I-S for non-fibrous NFs with very slow dissolution rates."		"Consider H-I-S for non-fibrous NFs with very slow dissolution rates."	"Consider H-I-Q/G for NFs showing instantaneous, quick or gradual dissolution."	"Consider H-I-Q/G for NFs showing instantaneous, quick or gradual dissolution."	"Consider H-O-x for oral exposure route."			
A4	group := 'NF **is** respirable, biopersistent, rigid HARN **with** potential **to** cause lung hazard'										X		X											
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23

function 'H-I-1'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_HARNs_CanDeposit_Info(tl).epqs	X
A2	result := result + DN_HARN_Dissolution_LSF_Info(tl).epqs	X
A3	result := result + DN_HARN_Dissolution_PSF_Info(tl).epqs	X
A4	result := result + DN_FibreLength_Info(tl).epqs	X
A5	result := result + DN_Rigid_Fibrous_Needles_Info(tl).epqs	X
A6	result := result + DN_Frustrated_Phagosytosis_Info(tl).epqs	X
A7	result := result + DG_HARN_Inflammation_Info(tl).epqs	X
A8	result := result + DG_HARN_Genotoxicity_Info(tl).epqs	X
		R1

Class 'H-I-2' is kind of 'H-I'

Hypothesis H-I-2: Respirable, biopersistent, rigid HARN: Following inhalation exposure and translocation of HARN to the pleura, mesothelioma development can occur.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-I-2"	
lead	: String	"HWU"	
description	: String	"Respirable, biopersistent, rigid HARN: Following inhalation exposure and translocation of HARN to the pleura, mesothelioma development can occur."	
rationale	: String	"Similar to hypothesis H-I-1, grouping of NFs according to the H-I-2 hypothesis may have a number of potential implications including facilitating the generation of a read-across argument for risk assessment which may allow waiving of testing for regulatory purposes (e.g. the completion of a registration dossier). Grouping according to the HARN mesothelioma hypothesis may also be used to guide and support the innovation of SbD materials or fill data gaps and increase scientific understanding of key mechanisms of fibre pathogenicity thereby further streamlining the risk assessment process in the future."	

Operators

function 'H-I-2'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman																						ELSE
C2	targ_NF	nil	ELSE																					–
C3	likely_exposure_routes	–	0	inhalation																			ELSE	–
C4	targ_NF.is_HARN	–	–	?	Yes																	ELSE	–	–
C5	targ_NF.DN_HARN_can_deposit_in_distal_region_of_lung	–	–	–	?	Yes															ELSE	–	–	–
C6	targ_NF.DN_HARNs_dissolve_very_slow_in_lung_lining_fluid	–	–	–	–	?	Yes													ELSE	–	–	–	–
C7	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	–	–	–	–	–	?	very_slow											ELSE	–	–	–	–	–
C8	targ_NF.DN_HARN_length_exceeds_5_micron	–	–	–	–	–	–	?	Yes									No	–	–	–	–	–	–
C9	targ_NF.DN_HARNs_are_rigid_and_needle_like	–	–	–	–	–	–	–	?	Yes							No	ELSE	–	–	–	–	–	–
C10	targ_NF.DN_HARNs_cause_frustrated_phagocytosis	–	–	–	–	–	–	–	–	?	Yes				No	ELSE	–	–	–	–	–	–	–	–
C11	source_material	–	–	–	–	–	–	–	–	–	nil		ELSE		–	–	–	–	–	–	–	–	–	–
C12	purpose	–	–	–	–	–	–	–	–	–	'regulatory'	ELSE	'regulatory'	ELSE	–	–	–	–	–	–	–	–	–	–
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	MI	MI	MI	MI	MI	INCL	INCL	INCL	INCL	EXCL	MI	EXCL	MI	EXCL	EXCL	EXCL	EXCL	IRR	IRR	IRR
A2	consequences→Add(#)										"Group as poorly soluble, rigid HARN with potential to cause mesothelioma"	"Group as poorly soluble, rigid HARN with potential to cause mesothelioma"	"Group as poorly soluble, rigid HARN with potential to cause mesothelioma"	"Group as poorly soluble, rigid HARN with potential to cause mesothelioma"	"Macrophage uptake "		"Agglomeration into tangled structures or fibre buckling during phagocytosis allows complete uptake"		"Cleared through the pleural stomata"	"Dissolution in lysosomal fluid, breakage and shortening of long fibres."		"Deposition primarily in the upper airways, efficient mucociliary clearance"			
A3	consequences→Add(#)										"Regulatory: Read-across to source is not possible."	"Precautionary/ SbD: Assume HARN can cause inflammation and fibrosis or cancer."	"Perform read-across to source material for impaired clearance, chronic inflammation and mesothelioma formation."		"Consider alternative hypothesis for non-fibrous NFs with very slow dissolution rates."		"Consider potential systemic effects."		"Consider potential systemic effects."	"Consider alternative hypothesis for NFs showing instantaneous, quick or partial dissolution."	"Consider alternative hypothesis for NFs showing instantaneous, quick or partial dissolution."			
A4	group := 'NF **is** respirable, biopersistent, rigid HARN **with** potential **to** cause mesothelioma'										X	X	X	X										
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24

function 'H-I-2'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		–
A1	/* DN) Can NF deposit in the distal region of the lung? */	
A2	result := DN_HARNs_CanDeposit_Info(tl).epqs	X
A3	/* DN) Dissolution of NF in lung lining fluid is: */	
A4	result := result + DN_HARN_Dissolution_LSF_Info(tl).epqs	X
A5	/* DN) Dissolution of NF in lysosomal fluid is: */	
A6	result := result + DN_HARN_Dissolution_PSF_Info(tl).epqs	X
A7	/* DN) Average fibre length in µm: */	
A8	result := result + DN_FibreLength_Info(tl).epqs	X
A9	/* DN) Are NF fibres rigid with a needle like morphology? */	
A10	result := result + DN_Rigid_Fibrous_Needles_Info(tl).epqs	X
A11	/* DN) Does NF cause frustrated phagocytosis? */	
A12	result := result + DN_Frustrated_Phagosytosis_Info(tl).epqs	X
A13	result := result + DG_HARN_Inflammation_Info(tl).epqs	X
A14	result := result + DG_HARN_Genotoxicity_Info(tl).epqs	X
		R1

Class 'H-I-I' is kind of 'H-I'

Hypothesis H-I-I: Respirable NFs with an instantaneous dissolution: Following inhalation exposure, the toxicity is driven by and is therefore similar to those of the constituent ions or molecules.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-I-I"	
lead	: String	"BASF/RIVM"	
description	: String	"Respirable NFs with an instantaneous dissolution: Following inhalation exposure, the toxicity is driven by and is therefore similar to those of the constituent ions or molecules."	
rationale	: String	"Respirable NFs with an instantaneous dissolution rate: Following inhalation exposure, the toxicity is driven by and is therefore similar to those of the constituent ions or molecules."	

Operators

function 'H-I-I'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman						ELSE
C2	targ_matr as Nanoform | NM	nil	ELSE					-
C3	likely_exposure_routes	-	0	inhalation			ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_lung_lining_fluid	-	-	?	instantaneously	ELSE	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	INCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"Group as instantaneously dissolving NF"	"Consider hypothesis H-I-S, H-I-G and H-I-Q on very slowly, gradually or quickly dissolving NFs"		
A3	consequences→Add(#)				"NFs dissolving into ionic or molecular form before they reach the viable cells."			
A4	consequences→Add(#)				"Perform read across to ionic or molecular form."			
		R1	R2	R3	R4	R5	R6	R7

function 'H-I-I'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result→Add(WTG(EPQ(PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS)))	X
A2	result := result + DN_Dissolution_LSF_Info(tl).epqs	X
		R1

Class 'H-I-Q' is kind of 'H-I'

Hypothesis H-I-Q: Respirable NFs with a quick dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity, but there is no concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-I-Q"	
lead	: String	"BASF/RIVM"	
description	: String	"Respirable NFs with a quick dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity, but there is no concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release."	
rationale	: String	"Respirable NFs with a quick dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity, but there is no concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release."	

Operators

function 'H-I-Q'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman								ELSE
C2	targ_NF	nil	ELSE							-
C3	likely_exposure_routes	-	0	inhalation					ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	-	?	quick			ELSE	-	-
C5	source_material	-	-	-	nil		ELSE	-	-	-
C6	purpose	-	-	-	'regulatory'	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	INCL	INCL	INCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"Read across not possible."	"Assume NF and/or released ions or molecules can induce inflammation upon acture exposure."	"Assume target NF can induce similar toxicity compared to the source material following acute and repeated exposure. Both the NF and the ions or molecules contribute to the toxicity."	"Consider hypothesis H-I-S, H-I-G and H-I-I on very slowly, gradually or instantaneous dissolving NFs"		
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'H-I-Q'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result→Add(WTG(EPQ(PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS)))	X
A2	result := result + DN_Dissolution_PSF_Info(tl).epqs	X
A3	result := result + DG_Reactivity_Info(tl).epqs	X
A4	result := result + DG_Inflammation_Info(tl).epqs	X
		R1

Class 'H-I-G' is kind of 'H-I'

Hypothesis H-1-G: Respirable NFs with a gradual dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity and there is some concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-1-G"	
lead	: String	"BASF/RIVM"	
description	: String	"Respirable NFs with a gradual dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity and there is some concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release."	
rationale	: String	"Respirable NFs with a gradual dissolution rate: Following inhalation exposure both NFs and constituent ions or molecules may contribute to toxicity and there is some concern for accumulation. Toxicity (also) depends on the location of the ionic or molecular release."	

Operators

function 'H-I-G'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman									ELSE
C2	targ_NF	nil	ELSE								-
C3	likely_exposure_routes	-	0	inhalation						ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	-	?	gradual			ELSE		-	-
C5	source_material	-	-	-	nil		ELSE	-		-	-
C6	purpose	-	-	-	'precautionary', 'safe-by-design'	ELSE	-	-		-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	INCL	INCL	INCL	EXCL		IRR	IRR
A2	consequences→Add(#)				"Assume NF and/or released ions or molecules can induce inflammation upon acute exposure and assume NF can accumulate and induce chronic inflammation upon repeated exposure."		"Assume target NF can induce similar toxicity compared to the source material following acute and repeated exposure. Both the NF and the ions or molecules contribute to the toxicity."	"Consider hypothesis H-I-S, H-I-Q and H-I-I on very slowly, quick or instantaneous dissolving NFs"			
		R1	R2	R3	R4	R5	R6	R7		R8	R9

function 'H-I-G'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result→Add(WTG(EPQ(PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS)))	X
A2	result := result + DN_Dissolution_PSF_Info(tl).epqs	X
A3	result := result + DG_Reactivity_Info(tl).epqs	X
A4	result := result + DG_Inflammation_Info(tl).epqs	X
		R1

Class 'H-I-S' is kind of 'H-I'

Hypothesis H-I-S: Respirable NFs with a very slow dissolution rate: Following inhalation exposure, toxicity is driven by the NFs and accumulation of NFs in the lungs can lead to long-term toxicity.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-I-S"	
lead	: String	"BASF/RIVM"	
description	: String	"Respirable NFs with a very slow dissolution rate: Following inhalation exposure, toxicity is driven by the NFs and accumulation of NFs in the lungs can lead to long-term toxicity."	
rationale	: String	"Respirable NFs with a very slow dissolution rate: Following inhalation exposure, toxicity is driven by the NFs and accumulation of NFs in the lungs can lead to long-term toxicity."	

Operators

function 'H-I-S'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman								ELSE
C2	targ_NF	nil	ELSE							-
C3	likely_exposure_routes	-	0	inhalation					ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	-	?	very_slow			ELSE	-	-
C5	source_material	-	-	-	nil		ELSE	-	-	-
C6	purpose	-	-	-	'precautionary', 'safe-by-design'	ELSE	-	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	MI	INCL	INCL	INCL	EXCL	IRR	IRR

A2	consequences→Add(#)				"Assume NF can induce impaired clearance and chronic inflammation upon repeated exposure, potentially leading to fibrosis or cancer."		"Assume target NF can induce impaired clearance and can induce similar toxicity compared to the source material following both acute and repeated exposure."	"Consider hypothesis H-I-G, H-I-Q and H-I-I on very gradual, quick or instantaneous dissolving NFs"		
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'H-I-S'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result→Add(WTG(EPQ(PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS)))	X
A2	result := result + DN_Dissolution_PSF_Info(tl).epqs	X
A3	result := result + DG_Reactivity_Info(tl).epqs	X
A4	result := result + DG_Inflammation_Info(tl).epqs	X
		R1

Class 'H-O' is kind of HumanHypothesis

Well defined oral hypothesis classes.

Operators

function 'H-O'.NF_exposure_to_human_GI_tract_likely(): HypothesisOutcome

C1	scenario_type	stHuman								ELSE
C2	targ_NF	nil	ELSE							-
C3	likely_exposure_routes	-	oral	inhalation					ELSE	-
C4	targ_NF.DP_From(EPQU(PC_GRANULOMETRY::EP_AERODYNAMIC_EQ_SPHERE_DIAMETER, ·nm)) | dp_Dae	-	-	nil	dp_Dae.value_y < 3.0·µm	dp_Dae.value_y ≥ 3.0·µm		ELSE	-	-
A1	result	IRR	INCL	MI	EXCL	INCL		MI	IRR	IRR
		R1	R2	R3	R4	R5		R6	R7	R8

function 'H-O'::DN_Dissolution_GIF_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-I, H-O-Q1, H-O-Q3, H-O-G1, H-O-G2, H-O-G3, H-O-S1, H-O-S2, H-O-S3 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cascade in vitro dissolution assay coupled to size distribution analysis."	"(No suitable Tier 2 methods currently exist for this decision node)"	"In vivo toxicokinetic studies."	
A4	result.preferred_methods	"NANoREG SOP for dissolution and TEM (ISO/PRF 21363 or NANoREG SOP) CLS (ISO 13318) and PTA (ISO 19430) for size distribution analysis."		"Measuring absorption and tissue distribution (OECD TG 417)"	
A5	result.guidance_for_assay_selection	"NANoREG D2.08 SOP 06: This method includes the consecutive addition of simulant OGI fluids (saliva, stomach and intestine) to NFs in order to reflect the passage of food through the human oro-gastrointestinal tract during food passage. The measurement of the dissolution rate is required after at least 30 minutes of the addition of the intestinal simulant juice (corresponding to the sampling time of 155 minutes since the beginning of the test) according the EFSA guideline (EFSA2018). The method suggested is not currently standardized, but it has been validated as an SOP within an EU project (NANoREG) and it is under validation through the OECD Working Party on Manufactured Nanomaterials (WPMN) (ENV/CHEM/NANO(2019)5/ADD1) Standardized fluid compositions applicable to the cascade in vitro dissolution test are accessible from ISO documents or an EU project derived SOP (NANoREG D2.08 SOP 06; ISO/TR 19057 and DIN 19738). The dissolution unit expression is based on half-life (t1/2) following the calculation described in Keller et al (Sci Rep, 2020. 10(1): p. 458) and consistent with the first-order dissolution kinetics of the ISO method (ISO/TR 19057)"		"Guidance of the studies may be found on OECD TG 417 which is currently under revision within the NanoHarmony project in order to improve the guidance applicability on nanospecific issues. One of the main limitations, in the case of ingested NFs, is that the majority of the studies quantify the total content of corresponding ions or molecules within the considered organs or tissues by quantitative in bulk techniques only upon tissue mineralization (e.g., ICP-MS). Then, limited or only indirect information on particle durability can be extrapolated. Single molecule-based techniques (microscopy or single particle-ICP) may technically overcome such limitations, however, most of the information generally extracted are qualitative."	
A6	result.tier_escalation	"Tier 1 assays provide information on the durability of the NF in the OGI simulant fluids. Progress to Tier 3 (No suitable Tier 2 methods currently exist for this decision node) will be dependent on user needs (higher level of confidence in durability outcome) and on expert judgement."			
A7	/* Cascade in vitro digestion assay, NANoREG D2.08 SOP 06 */				
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated intestinal fluid')))	X			
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated intestinal fluid')))	X			
A10	result.epqs→Add(WTG(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Simulated intestinal fluid')))	X			
A11	/* TEM, ISO 21363 or NANoREG D2.10 SOP 02 */	X			
A12	result.epqs→Add(WTG(PER(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Simulated intestinal fluid'), slConstituentParticleLevel), 10.0·%)))	X			
A13	/* CLS, ISO 13318 (cummulative mass based size distribution) */	X			
A14	result.epqs→Add(WTG(PER(EPQM(PC_GRANULOMETRY::EP_DmPx_D1, 'Simulated intestinal fluid'), 10.0·%)))	X			
A15	/* PTA, ISO 19430 hydrodynamic number based size distribution */	X			
A16	result.epqs→Add(WTG(PER(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Simulated intestinal fluid'), 10.0·%)))	X			
A17	/* In vivo oral toxicokinetic study, OECD TG 417 */			X	
A18	result.epqs→Add(WTG(EPQ(HH_BASIC_TOX::EP_IN_VIVO_ACCUMULATION)))			X	
		R1	R2	R3	R4

function 'H-O'::DG_Reactivity_Intestinal_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q1, H-O-G1, H-O-S1 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Acellular ROS measurements"	"Measurement of reactive oxygen species and/or cellular oxidant measurements of oxidative stress on 2D/co-cultures/3D intestine culture models."	"In vivo oxidative stress measurements"	
A4	result.preferred_methods	"DCFH2-DA (GRACIOUS SOP), EPR (ISO 18827), FRAS (GRACIOUS SOP)"	"DCFH2-DA (NANoREG SOP); GSH depletion/ GSSG accumulation (Toxicol In Vitro, 1998. 12(6): p. 649-59); Lipid peroxidation (Nanotoxicology, 2020. 14(3): p. 388-403.) and HMOX.1 expression (Toxicol In Vitro, 2021. 74: p. 105161)"	"glutathione depletion and lipid peroxidation after oral acute or repeated exposure (OECD TG 420 and TG 408)."	
A5	result.guidance_for_assay_selection	"When conducting in vitro biochemical assays (cytotoxicity, inflammation, genotoxicity), it is useful to provide an understanding of the intrinsic NF reactivity (e.g., redox potential, radical formation) that may trigger toxicity in cellular models. Tier 1 focuses on acellular assessment of ROS production. A more thorough TTS for reactive oxygen species (ROS) and oxidative stress is under development and will be published later this year (McBeth et al., manuscript in preparation). The TTS for reactivity includes the following Tier 1, Tier 2 and Tier 3 methods.Tier 1 focuses on acellular assessment of ROS production. The use of a combination of assays for regulatory implications is recommended."	"Measurement of ROS and/or cellular oxidant measurements of oxidative stress are recommended as a biological indicator of NF reactivity.Tier 2 proposes methods to confirm the NF ROS production/oxidative damage on cells after the positive outcome from Tier 1 acellular assays. DCFH2-DA (NANoREG D5.06 SOP 03) to assess the presence of ROS in cellular intestine 2D/cocultures/3D models following a single short term (24h) or repeated exposure to a range of NF concentrations. This assay is suitable tends to provide a negative (no ROS) or positive (ROS identified) answer but does not seem to be sufficiently sensitive to determine values in between. A variety of assays are currently under evaluation, including glutathione (GSH) antioxidant depletion and glutathione disulfide (GSSG) accumulation at short time points, lipid peroxidation and heme oxygenase 1 (HMOX-1) expression. Again, such assays could be conducted using intestine 2D/co-cultures/3D models following a single short term (24h) or repeated exposure to a range of NF concentrations."	"Glutathione (GSH) depletion and Lipid peroxidation are the common assays used to assess the in vivo oxidative stress. There are no standardized or validated method to suggest. These assays have to be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). Lipid peroxidation is the degradation of lipids that occurs as a result of oxidative damage resulting with the production of malondialdehyde (MDA). GSH plays a key role in many biological processes, such as the protection of cells against oxidation. The assay measure glutathione (GSH), and oxidized glutathione (GSSG) to get the ratio that is indicative of oxidative damge. Both the assays could be conducted in whole blood, serum, plasma and urine."	
A6	result.tier_escalation	"Measurement of ROS and/or cellular oxidant measurements of oxidative stress : Tier 2 will not necessarily provide a higher level of confidence in the grouping of similar NFs but may be more predictive of a physiologically relevant hazard outcome or provide more mechanistic insights. Therefore, progression to Tier 2 will depend on what the user wants (increase confidence in hazard response or not)."	"Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s) have the potential to induce ROS production or a cellular oxidant response. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* EPR; ISO TS 18827(ISO 2017) */	X			
A8	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY))))	X			
A9	/* FRAS; GRACIOUS SOP */	X			
A10	result.epqs→Add(TITLE("sBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE))))	X			
A11	result.epqs→Add(TITLE("mBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE))))	X			
A12	/* DCFH2-DA; GRACIOUS SOP */	X			
A13	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU))))	X			
A14	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU))))	X			
A15	/* DCFH2-DA; NANoREG SOP */		X		
A16	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL)))		X		
A17	/* Glutathione (GSH) assay */		X		
A18	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION)))		X		
A19	/* Lipid peroxidation (MDA) assay, EP_INVITRO_OXIDATIVE_STRESS_MDA_QUANTIFICATION? */		X		
A20	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_MDA_LIPID_PEROXIDATION)))		X		
A21	/* Heme oxigenase 1 (HMOX) assay */		X		
A22	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_IN_VITRO_HMOX_OXIDATIVE_STRESS_NFOLD_NEG_CONTROL)))		X		
A23	/* Acute oral toxicity; OECD TG 420 + measurement of oxidative stress */			X	
A24	/* Repeated dose 90 day oral toxicity; OECD TG 408 + measurement of oxidative stress */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Reactivity_Bacterial_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q3, H-O-G3, H-O-S3 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Acellular ROS measurements"	"Measurement of reactive oxygen species on 2D/ 3D bacteria culture models"		
A4	result.preferred_methods	"DCFH2-DA (GRACIOUS SOP), EPR (ISO 18827), FRAS (GRACIOUS SOP) "	"DCFH2-DA (NANoREG SOP) "		
A5	result.guidance_for_assay_selection	"When conducting in vitro biochemical assays (i.e. cytotoxicity) it is useful to provide an understanding of the intrinsic NF reactivity (e.g., redox potential, radical formation) that may trigger toxicity in bacteria models. Tier 1 focuses on acellular assessment of ROS production. If the aim is the SbD we recommended the use of a combination of assays for a broader assessment of reactivity, however if there are regulatory purposes (e.g. read-across) one test, the one more relevant for the selected NF(s), is considered sufficient."	"Measurement of ROS is recommended as a biological indicator of NF reactivity.Tier 2 proposes a validated method to confirm the NF reactivity after the positive outcome from Tier 1 acellular assays. DCFH2-DA (NANoREG D5.06 SOP 03) can be used to assess ROS in in vitro microbiota models (single strain bacterial cultures or multi-strain biofilms and in vitro microbiome models isolated from healthy individuals) following a single short term (24h) or repeated exposure for up to 5 days to a range of NF concentrations."		
A6	result.tier_escalation	"Measurement of ROS: Tier 2 will not necessarily provide a higher level of confidence in the grouping of similar NFs but may be more predictive of a physiologically relevant hazard outcome or provide more mechanistic insights. Therefore, progression to Tier 2 will depend on what the user wants (increase confidence in hazard response or not)."	"Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s) have the potential to induce ROS production Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* EPR; ISO TS 18827(ISO 2017) */	X			
A8	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY))))	X			
A9	/* FRAS; SOP in D5.3 of GRACIOUS */	X			
A10	result.epqs→Add(TITLE("sBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE))))	X			
A11	result.epqs→Add(TITLE("mBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE))))	X			
A12	/* DCFH2-DA; GRACIOUS SOP */	X			
A13	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU))))	X			
A14	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU))))	X			
A15	/* DCFH2-DA; NanoREG SOP */		X		
A16	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL)))		X		
		R1	R2	R3	R4

function 'H-O'::DG_Reactivity_Secondary_Organs_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-G2, H-O-S2 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Acellular ROS measurements"	"Measurement of reactive oxygen species and/or cellular oxidant measurements of oxidative stress on 2D/cocultures/3D cell culture models (secondary target organs)"	"In vivo oxidative stress measurements"	
A4	result.preferred_methods	"DCFH2-DA (GRACIOUS SOP), EPR (ISO 18827), FRAS (GRACIOUS SOP)"	"DCFH2-DA (NANoREG SOP); GSH depletion/ GSSG accumulation (Toxicol In Vitro, 1998. 12(6): p. 649-59); Lipid peroxidation (Nanotoxicology, 2020. 14(3): p. 388-403.) and HMOX.1 expression (Toxicol In Vitro, 2021. 74: p. 105161)"	"glutathione depletion and lipid peroxidation after oral acute or repeated exposure (OECD TG 420 and TG 408)."	
A5	result.guidance_for_assay_selection	"When conducting in vitro biochemical assays (cytotoxicity, inflammation, genotoxicity), it is useful to provide an understanding of the intrinsic NF reactivity (e.g., redox potential, radical formation) that may trigger toxicity in cellular models. Tier 1 focuses on acellular assessment of ROS production. If the aim is the SbD we recommended the use of a combination of assays for a broader assessment of reactivity, however if there are regulatory purposes (e.g. read-across) one test, the one more relevant for the selected NF(s), is considered sufficient."	"Measurement of ROS and/or cellular oxidant measurements of oxidative stress are recommended as a biological indicator of NF reactivity.Tier 2 proposes methods to confirm the NF ROS production/oxidative damage on cells after the positive outcome from Tier 1 acellular assays. DCFH2-DA (NANoREG D5.06 SOP 03) to assess the presence of ROS in cellular 2D/cocultures/3D models of secondary organs following a single short term (24h) or repeated exposure to a range of NF concentrations. This assay is suitable tends to provide a negative (no ROS) or positive (ROS identified) answer but does not seem to be sufficiently sensitive to determine values in between. A variety of assays are currently under evaluation, including glutathione (GSH) antioxidant depletion and glutathione disulfide (GSSG) accumulation at short time points, lipid peroxidation and heme oxygenase 1 (HMOX-1) expression. Again, such assays could be conducted using 2D/co-cultures/3D models of secondary organs following a single short term (24h) or repeated exposure to a range of NF concentrations."	"Glutathione (GSH) depletion and Lipid peroxidation are the common assays used to assess the in vivo oxidative stress. There are no standardized or validated method to suggest. These assays have to be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). Lipid peroxidation is the degradation of lipids that occurs as a result of oxidative damage resulting with the production of malondialdehyde (MDA). GSH plays a key role in many biological processes, such as the protection of cells against oxidation. The assay measure glutathione (GSH), and oxidized glutathione (GSSG) to get the ratio that is indicative of oxidative damge. Both the assays could be conducted in whole blood, serum, plasma and urine."	
A6	result.tier_escalation	"Measurement of ROS and/or cellular oxidant measurements of oxidative stress : Tier 2 will not necessarily provide a higher level of confidence in the grouping of similar NFs but may be more predictive of a physiologically relevant hazard outcome or provide more mechanistic insights. Therefore, progression to Tier 2 will depend on what the user wants (increase confidence in hazard response or not)."	"Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s) have the potential to induce ROS production or a cellular oxidant response . Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* EPR; ISO TS 18827(ISO 2017) */	X			
A8	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY))))	X			
A9	/* FRAS; GRACIOUS SOP */	X			
A10	result.epqs→Add(TITLE("sBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE))))	X			
A11	result.epqs→Add(TITLE("mBOD", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE))))	X			
A12	/* DCFH2-DA; GRACIOUS SOP */	X			
A13	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU))))	X			
A14	result.epqs→Add(TITLE("", WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU))))	X			
A15	/* DCFH2-DA; NANoREG SOP */		X		
A16	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL)))		X		
A17	/* Glutathione (GSH) assay */		X		
A18	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION)))		X		
A19	/* Lipid peroxidation (MDA) assay, EP_INVITRO_OXIDATIVE_STRESS_MDA_QUANTIFICATION? */		X		
A20	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_MDA_LIPID_PEROXIDATION)))		X		
A21	/* Heme oxigenase 1 (HMOX) assay */		X		
A22	result.epqs→Add(WTD(EPQ(HH_OXIDATIVE_STRESS::EP_IN_VITRO_HMOX_OXIDATIVE_STRESS_NFOLD_NEG_CONTROL)))		X		
A23	/* Acute oral toxicity; OECD TG 420 + oxidative stress measurement */			X	
A24					
A25	/* Repeated dose 90 day oral toxicity; OECD TG 408 + oxidative stress measurment */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Cytotoxicity_Intestinal_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q1, H-O-G1, H-O-S1 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cell viability measurements on 2D intestinal culture models"	"Cell viability measurements on co-cultures or 3D intestinal culture models"	"In vivo cytotoxicity measurements"	
A4	result.preferred_methods	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"Bodyweight and organ gross necropsy of target organ after oral acute or repeated exposure (OECD TG 420 or TG 408)"	
A5	result.guidance_for_assay_selection	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"Bodyweight: Individual weights of animals should be determined shortly before the test substance is administered and at least weekly thereafter. Organ gross necropsy of target organs: All animals in the study shall be subjected to a full, detailed gross necropsy which includes careful examination of the external surface of the body and of the tissue of interest (i.e. intestine). These assays have to be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions)."	
A6	result.tier_escalation	"Tier 1 proposes standardized or validated methods to assess the NF toxicity by using 2D intestinal in vitro models. When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test. Tier 1 assays provide insights on cytotoxicity of the target NF induced on 2D intestinal model. Tier 1 indicates that the target NF induce local toxicity by cytotoxicity by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro intestinal models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo intestinal tissue is preferred."	"Tier 2 proposes standardized or validated methods to assess the NF citotoxicity by using co-cultures or 3D intestinal models. When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test.Tier 2 assays will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s) induce cytotoxicity effects. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* MTS cell viability assay, ISO 19007; NANoREG D5.07 SOP 08 */	X	X		
A8	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A9	/* Alamar Blue Metabolic Cell Viability Assay; NANoREG D5.07 SOP 06 */	X	X		
A10	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A11	/* Lactate DeHydrogenase Assay; NANoREG D2.08 SOP 07 */	X	X		
A12	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A13	/* Neutral Red */	X			
A14	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM)))	X			
A15	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_VIABILITY_PERC_OF_CONTROL)))	X			
A16	/* Acute oral toxicity; OECD TG 420 + ?? */			X	
A17					
A18	/* Repeated dose 90 day oral toxicity; OECD TG 408 + ?? */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Cytotoxicity_Bacterial_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q3, H-O-G3, H-O-S3 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Viabiity measurements on 2D bacteria models"	"Viability measurements on 3D bacteria models"	"DNA sequencing of gut microbiota"	
A4	result.preferred_methods	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"measuring the decrease or increase of some bacteria species in the microbiota population after oral acute or repeated exposure (OECD TG 420 and TG 408)"	
A5	result.guidance_for_assay_selection	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"DNA sequencing of gut microbiota is performed by genomic DNA extraction and bacterial gene amplification of the Total gut microbiota community after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). There is no standardazided or validated method. This technique allows to derive alteration in the microbiota population such as a decrease or increase of some bacteria species."	
A6	result.tier_escalation	"Tier 1 proposes standardized or validated methods to assess the NF toxicity by using 2D single-species bacterial models. When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test. Tier 1 assays provide insights on cytotoxicity of the target NF induced on 2D bacterial models Tier 1 indicates that the target NF induce local toxicity by cytotoxicity by using 2D in vitro bacteria models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo intestinal tissue is preferred."	"Tier 2 proposes standardized or validated methods to assess the NF citotoxicity by using 3D bacteria models (dual- or multi-strain cultures and biofilm models of human commensal bacteria) When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test.Tier 2 assays will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s)induce cytotoxicity effects. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* MTS cell viability assay; ISO 19007; NANoREG D5.07 SOP 08 */	X	X		
A8	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A9	/* Alamar Blue Metabolic Cell Viability Assay; NANoREG D5.07 SOP 06 */	X	X		
A10	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A11	/* Lactate DeHydrogenase Assay; NANoREG D2.08 SOP 07 */	X	X		
A12	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A13	/* Neutral Red */	X			
A14	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM)))	X			
A15	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_VIABILITY_PERC_OF_CONTROL)))	X			
A16	/* NOTE.. Oral Acute is mentioned but not in matrix overview!*/			X	
A17	/* Repeated dose 90 day oral toxicity; OECD TG 408 + GUT microbiota DNA sequencing */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Cytotoxicity_Secondary_Organs_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-G2, H-O-S2 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cell viability measurements on 2D cell culture models (secondary target organs)"	"Cell viability measurements on co-cultures or 3D cell culture models (secondary target organs)"	"In vivo cytotoxicity measurements"	
A4	result.preferred_methods	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"MTS, LDH, Alamar Blue, Neutral Red (ISO 19007 and NANoREG SOPs)"	"Bodyweight and organ gross necropsy of target organ after oral acute or repeated exposure (OECD TG 420 or TG 408)."	
A5	result.guidance_for_assay_selection	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"The gastrointestinal area is mechanically protected by the epithelium and a layer of mucus. An intestinal tissue injury or damage could determine a measurable change in the biological equilibrium within the OGI tract but also particles penetration into the body. Currently, a wide range of cytotoxicity assays are available. Here we suggest three of the most used methods for defining NF cytotoxicity, such as the lactate dehydrogenase (LDH) assay that measure plasma membrane damage (NANoREG D2.08 SOP 07), the Alamar Blue (NANoREG D5.07 SOP 06) or MTS assays (ISO 19007) that measure both the mitochondrial enzyme function and lastly the Neutral red assay (NANoREG D5.07 SOP 06) that measure the endosome integrity. These assays can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for cytotoxicity includes the following Tier 1, Tier 2 and Tier 3 methods. When available, the standardized methods should be preferred upon validated assays.This endpoint should be addressed using a proper doses and exposure regimes to reflect a realistic human exposure scenario, when possible. For instance, when direct oral exposure is expected by food grade NFs, doses mimicking daily intake values are preferred, in association with repeated exposure to simulate long-term toxicological outcomes."	"Bodyweight: Individual weights of animals should be determined shortly before the test substance is administered and at least weekly thereafter. Organ gross necropsy of target organ: All animals in the study shall be subjected to a full, detailed gross necropsy which includes careful examination of the external surface of the body and of the tissue of interest (i.e., target secondary organs, such as liver, kidneys etc) These assays have to be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions)."	
A6	result.tier_escalation	"Tier 1 proposes standardized or validated methods to assess the NF toxicity by using 2D in vitro models of secondary target organs. When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test. Tier 1 assays provide insights on cytotoxicity of the target NF induced on 2D models of secondary target organs. Tier 1 indicates that the target NF induce local toxicity by cytotoxicity by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo secondary tissues is preferred."	"Tier 2 proposes standardized or validated methods to assess the NF citotoxicity by using co-cultures or 3D models (secondary target organs cells). When more than one method is proposed the user can choose the most appropriate assay depending on the chemical composition of the target NF in order to avoid interference of the NF with the test.Tier 2 assays will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s)induce cytotoxicity effects. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* MTS cell viability assay; ISO 19007; NANoREG D5.07 SOP 08 */	X			
A8	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A9	/* Alamar Blue Metabolic Cell Viability Assay; NANoREG D5.07 SOP 06 */	X			
A10	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A11	/* Lactate DeHydrogenase Assay NANoREG D2.08 SOP 07 */	X			
A12	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL)))	X			
A13	/* Neutral Red */	X			
A14	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM)))	X			
A15	result.epqs→Add(WTD(EPQ(HH_CYTOTOXICITY::EP_NRU_VIABILITY_PERC_OF_CONTROL)))	X			
A16	/* Acute oral toxicity; OECD TG 420 + ?? */			X	
A17	/* Repeated dose 90 day oral toxicity; OECD TG 408 + ?? */			X	
		R1	R2	R3	R4

function 'H-O'::DG_BarrierIntegrity_Intestinal_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q1, H-O-G1, H-O-S1 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Barrier damage measurements on 2D intestinal culture models"	"Barrier damage measurements on co-cultures or 3D intestinal culture models"	"In vivo barrier damage measurements"	
A4	result.preferred_methods	"TEER (NANoREG SOP)"	"TEER (NANoREG SOP)"	"Intestine gross necropsy after oral acute or repeated exposure (OECD TG 420 and TG 408)."	
A5	result.guidance_for_assay_selection	"Translocation of ingested NF through the intestinal barrier is a complex phenomenon that involves their diffusion through the mucus layer, paracellular transport through inter-epithelial tight junctions and contact with M-cells that regulate the transcytosis. Hence, damage to the intestinal barrier needs to be considered when testing NF adverse effects. To monitor the loss of the ability for the intestinal tissue to maintain its integrity, transepithelial electrical resistance (TEER) could be a useful in vitro replacement of the in vivo histopathologic analysis that qualitative measure the tissue damage. This assay can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect a standardised method. The TTS for barrier integrity includes the following Tier 1, Tier 2 and Tier 3 methods."	"Translocation of ingested NF through the intestinal barrier is a complex phenomenon that involves their diffusion through the mucus layer, paracellular transport through inter-epithelial tight junctions and contact with M-cells that regulate the transcytosis. Hence, damage to the intestinal barrier needs to be considered when testing NF adverse effects. To monitor the loss of the ability for the intestinal tissue to maintain its integrity, transepithelial electrical resistance (TEER) could be a useful in vitro replacement of the in vivo histopathologic analysis that qualitative measure the tissue damage. This assay can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect a standardised method. The TTS for barrier integrity includes the following Tier 1, Tier 2 and Tier 3 methods."	"Intestine gross necropsy: All animals in the study shall be subjected to a full, detailed intestine gross necropsy to identy any structural damage to the intestinal barrier. This assay has to be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions)."	
A6	result.tier_escalation	"Tier 1 proposes a validated method to assess the NF toxicity by using 2D intestinal in vitro models. Tier 1 assays provide insights on barrier damage induced by the target NF on 2D intestinal models. Tier 1 indicates that the target NF induce local toxicity by intestinal barrier impairment by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo intestinal tissue is preferred."	"Tier 2 proposes a validated methods to assess if NF affect the barrier integrity of co-cultures or the 3D intestinal models. Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s)induce an intestinal barrier damage. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* TransEpithelial Electrical Resistance (TEER) assay; NANoREG D5.03 DR, SOP 03 */	X	X		
A8	result.epqs→Add(WTD(EPQ(HH_BARRIER_INTEGRITY::EP_INVITRO_BARRIER_INTEGRITY)))	X			
A9	result.epqs→Add(WTD(EPQ(HH_BARRIER_INTEGRITY::EP_TEER_DECREASE_VERSUS_CONTROL)))	X			
A10	/* Intestine gross necropsy after oral acute or repeated exposure (OECD TG 420 and TG 408) */			X	
A11					
		R1	R2	R3	R4

function 'H-O'::DG_BarrierIntegrity_Bacterial_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q3, H-O-G3, H-O-S3 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Barrier damage measurements on 2D bacterial models"	"Barrier damage measurements on 3D bacteria models"	"DNA sequencing of gut microbiota"	
A4	result.preferred_methods	"AFM (ACS Appl Mater Interfaces, 2016. 8(7): p. 4963-76.)"	"AFM (ACS Appl Mater Interfaces, 2016. 8(7): p. 4963-76.)"	"Measuring the structure damage of some bacteria species in the microbiota population after oral acute or repeated exposure (OECD TG 420 and TG 408)"	
A5	result.guidance_for_assay_selection	"Translocation of ingested NF through the intestinal barrier is a complex phenomenon that involves their diffusion through the mucus layer, paracellular transport through inter-epithelial tight junctions and contact with M-cells that regulate the transcytosis. Hence, damage to the intestinal barrier and therefore also to the intestinal microbiota needs to be considered when testing NF adverse effects. As there are no SOPs available for testing bacterial cell wall damage of single-species bacterial cultures, we suggest using a microscope technique. When possible, atomic force microscopy (AFM) imaging is proposed. However other suitable microscopy techniques can be selected by the user"	"Translocation of ingested NF through the intestinal barrier is a complex phenomenon that involves their diffusion through the mucus layer, paracellular transport through inter-epithelial tight junctions and contact with M-cells that regulate the transcytosis. Hence, damage to the intestinal barrier and therefore also to the intestinal microbiota needs to be considered when testing NF adverse effects. As there are no SOPs available for testing bacterial cell wall, cell of multi-strain biofilms and in vitro microbiome models isolated from healthy individuals, we suggest using a microscope technique, when possible. Atomic force microscopy (AFM) imaging is proposed. However other suitable techniques can be selected by the user."	"DNA sequencing of gut microbiota is performed by genomic DNA extraction and bacterial gene amplification of the Total gut microbiota community after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). There is no standardazided or validated method. This technique allows to derive alteration in the microbiota population, such as structure damage of some bacteria species."	
A6	result.tier_escalation	"Tier 1 proposes a microscope technique to assess the NF toxicity by using 2D bacteria vitro models. Tier 1 assays provide insights on barrier damage induced by the target NF on 2D bacteria models. Tier 1 indicates that the target NF induce local toxicity by damaging the bacteria cell wall by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo intestinal tissue is preferred."	"Tier 2 proposes a microscope technique to assess if NF affect the barrier integrity of co-cultures or the 3D models. Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s)induce a barrier damage. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* AFM; No SOP, ACS Appl Mater Interfaces, 2016. 8(7): p. 4963-76. */	X	X		
A8	result.epqs→Add(WTD(EPQ(HH_BARRIER_INTEGRITY::EP_IN_VITRO_INTESTINAL_MICROBIOTA_INTEGRITY)))	X	X		
A9	/* Repeated dose 90 day oral toxicity; OECD TG 408, → EP_MICROBIOTA DNA SEQUENCING */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Inflammation_Intestinal_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q1, H-O-G1, H-O-S1 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cytokine secretion measurements on 2D intestinal culture models"	"Cytokine secretion measurements on co-cultures or 3D intestinal culture models"	"In vivo inflammation measurements"	
A4	result.preferred_methods	"ELISA (NANoREG SOP)"	"ELISA (NANoREG SOP)"	"hematology test and inflammatory markers evaluation (ELISA assay) in blood after oral acute or repeated exposure (OECD TG 420 or TG 408)"	
A5	result.guidance_for_assay_selection	"Another important key endpoint for measuring the level of NF local toxicity is the induction of a pro-inflammatory response. In in vivo studies, inflammation is commonly monitored by immunohistochemical staining or by quantifying the inflammatory serum biomarkers (e.g., cytokines, C-reactive protein etc). The most used in vitro assay that measures the activation of a pro-inflammatory response is the use of ELISA methods to determine of the amount of proinflammatory cytokines (e.g., IL-6, IL8 and TNF-alpha) secreated by the cells. This assay can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for inflammation includes the following Tier 1, Tier 2 and Tier 3 methods."	"Another important key endpoint for measuring the level of NF local toxicity is the induction of a pro-inflammatory response. In in vivo studies, inflammation is commonly monitored by immunohistochemical staining or by quantifying the inflammatory serum biomarkers (e.g., cytokines, C-reactive protein etc). The most used in vitro assay that measures the activation of a pro-inflammatory response is the use of ELISA methods to determine of the amount of proinflammatory cytokines (e.g., IL-6, IL8 and TNF-alpha) secreated by the cells. This assay can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for inflammation includes the following Tier 1, Tier 2 and Tier 3 methods."	"In order to investigate the in vivo inflammatory response the blood of animals has to be collected after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). Differents parameters could be analyzed: hematology and inflammatory markers (i.e. cytokines). Hematology: total leukocyte count (WBC), lymphocytes (LYO), neutrophils (NEU) and monocytes (MONO) were quantify by a blood cell counter. Inflammatory markers: the determination of inflammatory cytokines is performed by ELISA assay."	
A6	result.tier_escalation	"Tier 1 proposes a validated method to assess the NF toxicity by using 2D intestinal in vitro models. Tier 1 assay provide insights on the level of inflammation induced by the target NF on 2D intestinal models. Tier 1 indicates that the target NF induce local toxicity by inducing a pro inflammatory response by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo intestinal tissue is preferred."	"Tier 2 proposes a validated methods to assess if NF induce a proinflammatory responses by using co-cultures or 3D intestinal models..Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s) induce a pro inflammatory response. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* ELISA assay; NANoREG D5 06 DR, SOP 06 */	X	X		
A8	/* Acute oral toxicity; OECD TG 420 + inflammatory markers? */			X	
A9	/* Repeated dose 90 day oral toxicity; OECD 408 + inflammatory markers? */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Inflammation_Secondary_Organs_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-G2, H-O-S2 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Cytokine secretion measurements on 2D cell culture models (secondary target organs)"	"Cytokine secretion measurements on co-cultures or 3D cell culture models (secondary target organs)"	"In vivo inflammation measurements"	
A4	result.preferred_methods	"ELISA (NANoREG SOP)"	"ELISA (NANoREG SOP)"	"hematology and inflammatory markers evaluation (ELISA assay) in blood after oral acute or repeated exposure (OECD TG 420 or TG 408)"	
A5	result.guidance_for_assay_selection	"Another important key endpoint for measuring the level of NF systemic toxicity is the induction of a pro-inflammatory response. In in vivo studies, inflammation is commonly monitored by immunohistochemical staining or by quantifying the inflammatory serum biomarkers (e.g., cytokines, C-reactive protein etc). The most used in vitro assay that measures the activation of a pro-inflammatory response is the use of ELISA methods to determine of the amount of proinflammatory cytokines (e.g., IL-6, IL8 and TNF-alpha) secreated by the cells. This assay can be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. The TTS for inflammation includes the following Tier 1, Tier 2 and Tier 3 methods."	"Another important key endpoint for measuring the level of NF systemic toxicity is the induction of a pro-inflammatory response. In in vivo studies, inflammation is commonly monitored by immunohistochemical staining or by quantifying the inflammatory serum biomarkers (e.g., cytokines, C-reactive protein etc). The most used in vitro assay that measures the activation of a pro-inflammatory response is the use of ELISA methods to determine of the amount of proinflammatory cytokines (e.g., IL-6, IL8 and TNF-alpha) secreated by the cells."	"In order to investigate the in vivo inflammatory response the blood of animals has to be collected after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). Differents parameters could be analyzed: hematology and inflammatory markers (i.e. cytokines). Hematology: total leukocyte count (WBC), lymphocytes (LYO), neutrophils (NEU) and monocytes (MONO) were quantify by a blood cell counter. Inflammatory markers: the determination of inflammatory cytokines is performed by ELISA assay."	
A6	result.tier_escalation	"Tier 1 proposes a validated method to assess the NF toxicity by using 2D in vitro models of secondary target organs. Tier 1 assay provide insights on the level of inflammation induced by the target NF on 2D models of secondary target organs. Tier 1 indicates that the target NF induce systemic toxicity by inducing a pro inflammatory response by using 2D in vitro models. Information from Tier 2 can be used to support the outcomes of Tier 1 by using complex in vitro models (3D models that are more physiologically-relevant) and will be dependent on user needs (increase confidence in hazard response or not) and on expert judgement. With this respect, the use of physiologically relevant in vitro models to better resemble the characteristics of in vivo secondary tissues is preferred."	"Tier 2 proposes a validated methods to assess if NF induce a proinflammatory responses by using co-cultures or 3D models. Tier 2 assay will provide more information in a more physiologically-relevant context compared to Tier1 supporting the outcome that the target NF(s)induce a pro inflammatory response. Progression to Tier 3 will be dependent on user needs (higher level of confidence in toxicity outcome) and on expert judgement."		
A7	/* ELISA assay; NANoREG D5 06 DR, SOP 06 */	X	X		
A8	/* Acute oral toxicity; OECD TG 420 + inflammatory markers */			X	
A9	/* Repeated dose 90 day oral toxicity; OECD TG 408 + inflammatory markers */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Genotoxicity_Intestinal_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-Q1, H-O-G1, H-O-S1 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Genotoxicity damage measurements on 2D intestinal culture models"	"Genotoxicity damage measurements on co-cultures or 3D intestinal culture models "	"In vivo genotoxicity measurements"	
A4	result.preferred_methods	"Gene mutation assays (OECD TG 476 and TG 490) and chromosomal damage assays (OECD TG 487 and OECD TG 473)"	"chromosomal damage assay (OECD TG 487), comet or histone H2AX phosphorylation assays (PATROLS SOPs)"	"TGR mutation assays (OECD TG 488), quantification of micronuclei (OECD TG 474), evaluation of the DNA strand breaks by alkaline comet assay, OECD TG 489) after oral acute or repeated exposure (OECD TG 420 and TG 408)"	
A5	result.guidance_for_assay_selection	"NF ingestion can also induce local genotoxicity responses, A more detailed TTS for this decision node has been developed (Verdon et al 2021 submitted). The Tier 1 and Tier 2 proposed a list of genotoxicity assays from the OECD guidelines to be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. However, moving toward Tier 2 is recommended for a better understanding of secondary DNA damage."	"NF ingestion can also induce local genotoxicity responses, A more detailed TTS for this decision node has been developed (Verdon et al 2021 submitted). The Tier 1 and Tier 2 proposed a list of genotoxicity assays from the OECD guidelines to be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. However, moving toward Tier 2 is recommended for a better understanding of secondary DNA damage."	"Different assays have been proposed but one test is considered sufficient. These assays should be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). The OECD 474 test is used for the detection of damage induced by the test material to the chromosomes or the mitotic apparatus of erythroblasts. The test evaluates micronucleus formation in erythrocytes sampled either in the bone marrow or peripheral blood cells of animals. The OECD 489 is used for the detection of DNA strand breaks in cells or nuclei isolated from intestine tissue. The OECD 488 test assess germ cell and somatic cell mutagenicity using transgenic rodent (TGR) models from the tissue of interest."	
A6	result.tier_escalation	"The Tier 1 proposed a list of genotoxicity assays from the OECD guidelines to be conducted As recommended by OECD guidelines, when there is a positive outcome from a single in vitro study, the user should go through the Tier 3 level."	"The Tier 2 proposed a list of genotoxicity assays from the OECD guidelines to be conducted As recommended by OECD guidelines, when there is a positive outcome from a single in vitro study, the user should go through the Tier 3 level."		
A7	/* In Vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes; OECD TG 476 */	X	X		
A8	/* In Vitro Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene; OECD TG 490 */	X	X		
A9	/* In Vitro Mammalian Cell Micronucleus test; OECD TG 487 */	X	X		
A10	/* In Vitro Mammalian Chromosomal Aberration Test; OECD TG 473 */	X	X		
A11	/* Mammalian Erythrocyte Micronucleus Test; OECD TG 474 */			X	
A12	/* In Vivo Mammalian Alkaline Comet Assay; OECD TG 489 */			X	
A13	/* Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays; OECD TG 488 */			X	
		R1	R2	R3	R4

function 'H-O'::DG_Genotoxicity_Secondary_Organs_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* H-O-G2, H-O-S2 */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Genotoxicity damage measurements on 2D cell culture models (secondary target organs)"	"Genotoxicity damage measurements on co-cultures or 3D cell culture models (secondary target organs)"	"In vivo genotoxicity measurements"	
A4	result.preferred_methods	"Gene mutation assays (OECD TG 476 and TG 490) and chromosomal damage assays (OECD TG 487 and OECD TG 473)"	"Chromosomal damage assay (OECD TG 487), comet or histone H2AX phosphorylation assays (PATROLS SOPs)"	"TGR mutation assays (OECD TG 488), quantification of micronuclei (OECD TG 474), evaluation of the DNA strand breaks by alkaline comet assay (OECD TG 489) after oral acute or repeated exposure (OECD TG 420 and TG 408)"	
A5	result.guidance_for_assay_selection	"NF ingestion can also induce systemic genotoxicity responses, thus in vitro genotoxicity assays should be performed to investigate the systemic toxicity."	"NF ingestion can also induce systemic genotoxicity responses, A more detailed TTS for this decision node has been developed (Verdon et al 2021 submitted). The Tier 1 and Tier 2 proposed a list of genotoxicity assays from the OECD guidelines to be conducted using a range of in vitro cell models, which can be chosen by the user to reflect either a standardised method or a specific tissue target. However, moving toward Tier 2 is recommended for a better understanding of secondary DNA damage."	" Different assays have been proposed but one test is considered sufficient. These assays should be performed after oral acute or repeated exposure (refer to OECD TG 420 and TG 408 for details in exposure conditions). The OECD 474 test is used for the detection of damage induced by the test material to the chromosomes or the mitotic apparatus of erythroblasts. The test evaluates micronucleus formation in erythrocytes sampled either in the bone marrow or peripheral blood cells of animals. The OECD 489 is used for the detection of DNA strand breaks in cells or nuclei isolated from secondary target tissues (i.e. liver, kidneys etc).The OECD 488 test assess germ cell and somatic cell mutagenicity using transgenic rodent (TGR) models from the tissue of interest."	
A6	result.tier_escalation	"The Tier 1 proposed a list of genotoxicity assays from the OECD guidelines to be conducted As recommended by OECD guidelines, when there is a positive outcome from a single in vitro study, the user should go through the Tier 3 level."	"The Tier 2 proposed a list of genotoxicity assays from the OECD guidelines to be conducted As recommended by OECD guidelines, when there is a positive outcome from a single in vitro study, the user should go through the Tier 3 level."		
A7	/* In Vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes; OECD TG 476 */	X	X		
A8	/* In Vitro Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene; OECD TG 490 */	X	X		
A9	/* In Vitro Mammalian Cell Micronucleus test; OECD TG 487 */	X	X		
A10	/* In Vitro Mammalian Chromosomal Aberration Test; OECD TG 473 */	X	X		
A11	/* Mammalian Erythrocyte Micronucleus Test; OECD TG 474 */			X	
A12	/* In Vivo Mammalian Alkaline Comet Assay; OECD TG 489 */			X	
A13	/* Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays; OECD TG 488 */			X	
		R1	R2	R3	R4

Class 'H-O-I' is kind of 'H-O'

Well defined oral hypothesis classes.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-I"	
lead	: String	"IIT (Luisana, Stefania)"	
description	: String	"NFs with an instantaneous dissolution: Following oral exposure, the toxicity is driven by and is therefore similar to that of the constituent ions or molecules."	
rationale	: String	"NFs can be grouped as instantaneously dissolving if they have a t 1/2 ≤ 10 minutes. As suggested in H-O-I, if a NF is instantaneously dissolving under conditions relevant for the human OGI physiology, generation of a non-nanomaterial form is expected. The IATA for H-O-I does not include any other DNs, but drives the user decision depending on the purpose of grouping. If the purpose is generation of a dossier to comply with relevant regulations then application of read across to non-nanomaterial forms with the soluble constituent ionic or molecular forms is proposed to be the most suitable; ii) if precautionary measures or SbD are requested, no nano-specific risk evaluation is needed, however, it may be possible to predict the hazard based on the hazard of constituent ions/molecules."	

Operators

function 'H-O-I'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman								ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL				EXCL	MI		ELSE	-
C3	likely_exposure_routes	-				-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids | t	?	instantaneously		ELSE	-	-	-	-	-
C5	purpose	-	'precautionary', 'safe-by-design'	ELSE	-	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	INCL	INCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)		"Group as instantaneously dissolving NF in OGI fluids."	"Group as instantaneously dissolving NF in OGI fluids"	"Consider hypothesis H-O-Q, H-O-S or H-O-G on quick, very slow or gradual dissolving NF"	"Negligible exposure to GI tract"				
A3	group := 'NF dissolves instantaneous **in** OGI fluids'		X	X						
A4	consequences→Add(#)		"Assume no NF specific toxicity."	"Perform read across to source material for oral toxicity"						
A5				/* "Should this be.. perform read across to ionic/molecular form?"*/						
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'H-O-I'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
		R1

Class 'H-O-Q1' is kind of 'H-O'

Hypothesis H-O-2: Oral uptake of NF characterized by high dissolution rate in the gastrointestinal tract will result in a dissolving NF with the potential to release soluble organic-molecular or ionic complexes that will lose nano-specific action.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-Q1"	
lead	: String	"ITT"	
description	: String	"NFs with a quick dissolution: Following oral exposure both NFs and constituent ions or molecules may contribute to local inflammation in the OGI tract, but there is no concern for NF accumulation."	
rationale	: String	"The 'quick dissolving' hypothesis deals with NFs that exhibit a t1/2 > 10 minutes but ≤2 hours in simulant OGI juices and that do not have the potential to accumulate as they have a t1/2 ≤ 48 hours in lysosomal simulant fluid. Local toxicity is assessed by several descriptors (i.e., PC surface properties, reactivity, inflammation, genotoxicity, cytotoxicity and barrier impairment) that can be differently analysed: for SbD/precautionary based grouping, a qualitative similarity assessment may be sufficient to assume, based on expert judgment, that the hazard (local toxicity) is driven by not accumulating NF (itself and/or its constituent ions or molecules). On the contrary, if the grouping is made in preparation of regulation, where read-across is expected, the H-O-Q1 IATA provides guidance for a quantitative similarity assessment by identifying NFs with similar chemical composition. The accompanying TTS provides a practical guidance on how to assess the 'target 'NF versus the ''source. Importantly, in line with ECHA guidelines (ECHA 2019) the oral IATAs indicate that the quantitative similarity assessment must be applied to all DNs in the IATA. Here, if the NF behaves very similarly in comparison to the identified ''source across all DNs, the similarity assessment is considered successful and poses the conditions for performing read across following the available regulatory guidelines. If the similarity is not accepted (NF and source material are not sufficiently similar for read across), the user, for SbD and precautionary, should assume hazard (local toxicity) is driven by NF (itself and/or its constituent ions or molecules) "	

Operators

function 'H-O-Q1'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman																	ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL														EXCL	MI		IRR	–
C3	likely_exposure_routes	–														–	oral	ELSE	–	–
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	quick												ELSE	–	–	–	–	–
C5	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	–	?	quick										ELSE		–	–	–	–	–
C6	source_material	–	–	nil				ELSE						–		–	–	–	–	–
C7	purpose	–	–	'precautionary', 'safe-by-design'		ELSE		'precautionary', 'safe-by-design'		'regulatory'		ELSE		'precautionary', 'safe-by-design'		ELSE	–	–	–	–	–
A1	**begin** outcome := #; result := outcome **end**	MI	MI	INCL		INCL		INCL		INCL		INCL		EXCL		EXCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Group as not biopersistent NFs"		"Group as not biopersistent NFs"		"Group as not biopersistent NFs"		"Group as not biopersistent NFs"		"Group as not biopersistent NFs"		"Biopersistence is expected."		"Biopersistence is expected."	"Consider hypothesis, H-O-I, H-O-G or H-O-S on instantaneous, gradual or very slow dissolving NF."					
A3	consequences→Add(#)			"Assume hazard (local toxicity) is driven by NF (itself and/or its constituent ions or molecules)."						"Perform read across to NF with similar chemical composition for local toxicity by the NF itself and constituent ions or molecules."				"Assume hazard (systemic toxicity) is driven by the release of constituent ions or molecules in secondary organs."						
A4	group := 'NF dissolves quick **in** OGI fluids'																				
		R1	R2	R3		R4		R5		R6		R7		R8		R9	R10	R11	R12	R13	R14	R15

function 'H-O-Q1'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Intestinal_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Intestinal_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Intestinal_Info(tl).epqs	X
A5	result := result + DG_Inflammation_Intestinal_Info(tl).epqs	X
A6	result := result + DG_Genotoxicity_Intestinal_Info(tl).epqs	X
		R1

Class 'H-O-Q3' is kind of 'H-O'

H-O-Q3: NFs with a quick dissolution: Following oral exposure both NFs and constituent ions or molecules may drive antimicrobial impacts (e.g., reducing microbial content and diversity within the OGI tract), but there is no concern for NF accumulation.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-Q3"	
lead	: String	"IIT (Luisana, Stefania)"	
description	: String	"NFs with a quick dissolution: Following oral exposure both NFs and constituent ions or molecules may drive antimicrobial impacts (e.g., reducing microbial content and diversity within the OGI tract), but there is no concern for NF accumulation."	
rationale	: String	"The ‘quick ’dissolving hypothesis deals with NFs that exhibit a t1/2 > 10 minutes but ≤2 hours in simulant OGI juices and that do not have the potential to accumulate as they have a t1/2 ≤ 48 hours in lysosomal simulant fluid. Microbiota dysbiosis is assessed by several descriptors (i.e., PC surface properties, reactivity, cytotoxicity and barrier impairment) that can be differently analysed: for SbD/precautionary based grouping, a qualitative similarity assessment may be sufficient to assume, based on expert judgment, that the hazard (microbiota dysbiosis) is driven by not accumulating NF (itself and/or its constituent ions or molecules). On the contrary, if the grouping is made in preparation of regulation, where read-across is expected, the H-O-Q3 IATA provides guidance for a quantitative similarity assessment by identifying NFs with similar chemical composition. The accompanying TTS provides a practical guidance on how to assess the ‘target ’NF versus the ‘’source. Importantly, in line with ECHA guidelines (ECHA 2019) the oral IATAs indicate that the quantitative similarity assessment must be applied to all DNs in the IATA. Here, if the NF behaves very similarly in comparison to the identified ‘’source across all DNs, the similarity assessment is considered successful and poses the conditions for performing read across following the available regulatory guidelines. If the similarity is not accepted (NF and source material are not sufficiently similar for read across), the user, for SbD and precautionary, should assume hazard (microbiota dysbiosis) is driven by NF (itself and/or its constituent ions or molecules)."	

Operators

function 'H-O-Q3'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman														ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL										EXCL	MI		IRR	-
C3	likely_exposure_routes	-										-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	quick							ELSE		-	-	-	-	-
C5	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	?	quick				ELSE		-		-	-	-	-	-
C6	source_material	-	-	nil		ELSE		-		-		-	-	-	-	-
C7	purpose	-	-	'precautionary', 'safe-by-design'	ELSE	'regulatory'	ELSE	'precautionary', 'safe-by-design'	ELSE	-		-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	MI	INCL	INCL	INCL	INCL	EXCL	EXCL	EXCL		IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Group as not biopersistence NFs."	"Group as not biopersistence NFs."	"Group as not biopersistence NFs."	"Group as not biopersistence NFs."	"NF biopersistence is expected."	"NF biopersistence is expected."	"Consider hypothesis, H-O-I, H-O-G or H-O-S on instantaneous, gradual or very slow dissolving NF."						
A3	consequences→Add(#)			"Assume hazard (microbiota dysbiosis) is driven by NF (itself and/or its constituent ions or molecules)"		"Perform read across to NF with similar chemical composition for microbiota dysbiosis by NFs and constituent ions or molecules."		"Assume hazard (microbiota dysbiosis) si driven by the release of constituent ions or molecules."								
A4	group := 'None biopersistent NF dissolves quick **in** OGI fluids'			X												
		R1	R2	R3	R4	R5	R6	R7	R8	R9		R10	R11	R12	R13	R14

function 'H-O-Q3'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Bacterial_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Bacterial_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Bacterial_Info(tl).epqs	X
		R1

Class 'H-O-G1' is kind of 'H-O'

H-O-G1: NFs showing gradual dissolution: Following oral exposure both NFs and constituent ions or molecules may lead to local inflammation in the GIT.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-G1"	
lead	: String	"IIT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs showing gradual dissolution: Following oral exposure both NFs and constituent ions or molecules may lead to local inflammation in the GIT."	
rationale	: String	"For the group of 'gradual 'dissolving NFs (H-O-G), both the NF (potentially with reduced size) and the soluble form of the material co-exist. To be grouped as gradual dissolving the NF must exhibit a t1/2 between 2 hours and 60 hours in the OGI simulant fluids. Local toxicity is assessed by several descriptors (i.e., PC surface properties, reactivity, inflammation, genotoxicity, cytotoxicity and barrier impairment) that can be differently analysed: for SbD/precautionary based grouping, a qualitative similarity assessment may be sufficient to assume, based on expert judgment, that the hazard (local toxicity) is driven by not accumulating NF (itself and/or its constituent ions or molecules). On the contrary, if the grouping is made in preparation of regulation, where read-across is expected, the H-O-G1 IATA provides guidance for a quantitative similarity assessment by identifying NFs with similar chemical composition. The accompanying TTS provides a practical guidance on how to assess the 'target 'NF versus the ''source. Importantly, in line with ECHA guidelines (ECHA 2019) the oral IATAs indicate that the quantitative similarity assessment must be applied to all DNs in the IATA. Here, if the NF behaves very similarly in comparison to the identified ''source across all DNs, the similarity assessment is considered successful and poses the conditions for performing read across following the available regulatory guidelines. If the similarity is not accepted (NF and source material are not sufficiently similar for read across), the user, for SbD and precautionary, should assume hazard (local toxicity) is driven by NF (itself and/or its constituent ions or molecules)."	

Operators

function 'H-O-G1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman							ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL			EXCL	MI		IRR	-
C3	likely_exposure_routes	-			-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	gradual	ELSE	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	INCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Consider hypothesis H-O-Q, H-O-S or H-O-I on quick, very slow and instantaneous dissolving NF"					
A3	group := 'NF dissolves gradually **in** OGI fluids'		X						
		R1	R2	R3	R4	R5	R6	R7	R8

function 'H-O-G1'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Intestinal_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Intestinal_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Intestinal_Info(tl).epqs	X
A5	result := result + DG_Inflammation_Intestinal_Info(tl).epqs	X
A6	result := result + DG_Genotoxicity_Intestinal_Info(tl).epqs	X
		R1

Class 'H-O-G2' is kind of 'H-O'

H-O-G2: NFs showing gradual dissolution : Following oral exposure both NFs and constituent ions or molecules may translocate to secondary target organs and may lead to systemic toxicity in secondary organs.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-G2"	
lead	: String	"IIT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs showing gradual dissolution : Following oral exposure both NFs and constituent ions or molecules may translocate to secondary target organs and may lead to systemic toxicity in secondary organs."	
rationale	: String	"For the group of ‘gradual ’dissolving NFs (H-O-G), both the NF (potentially with reduced size) and the soluble form of the material co-exist. To be grouped as gradual dissolving and biopersistent (H-O-G2), the NF must exhibit a t1/2 between 2 hours and 60 hours in the OGI simulant fluids, whereas, in simulant lysosomal fluid, they must have a t1/2 greater than 48 hours and less than 1440 hours. Systemic toxicity is assessed by several descriptors (i.e., PC surface properties, reactivity, inflammation, genotoxicity and cytotoxicity) that can be differently analysed: for SbD/precautionary based grouping, a qualitative similarity assessment may be sufficient to assume, based on expert judgment, that the hazard (local toxicity) is driven by not accumulating NF (itself and/or its constituent ions or molecules). On the contrary, if the grouping is made in preparation of regulation, where read-across is expected, the H-O-G2 IATA provides guidance for a quantitative similarity assessment by identifying NFs with similar chemical composition. The accompanying TTS provides a practical guidance on how to assess the ‘target ’NF versus the ‘’source. Importantly, in line with ECHA guidelines (ECHA 2019) the oral IATAs indicate that the quantitative similarity assessment must be applied to all DNs in the IATA. Here, if the NF behaves very similarly in comparison to the identified ‘’source across all DNs, the similarity assessment is considered successful and poses the conditions for performing read across following the available regulatory guidelines. If the similarity is not accepted (NF and source material are not sufficiently similar for read across), the user, for SbD and precautionary, should assume hazard (local toxicity) is driven by NF (itself and/or its constituent ions or molecules)."	

Operators

function 'H-O-G2'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman										ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL						EXCL	MI		IRR	-
C3	likely_exposure_routes	-						-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	gradual				ELSE	-	-	-	-	-
C5	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	?	gradual	ELSE		-	-	-	-	-	-
C6	purpose	-	-	-	'precautionary', 'safe-by-design'	ELSE	-	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	MI	INCL	EXCL	EXCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)				"No systemic toxicity is expected by NF biopersistence."	"No systemic toxicity is expected by NF biopersistence."	"Consider hypothesis H-O-Q, H-O-S or H-O-I on quick, very slow and instantaneous dissolving NF."					
A3	consequences→Add(#)				"Assume hazard is driven by NF that can cause systemic toxicity due to highly biopersistence and ion release in secondary organs."							
A4	group := 'Biopersistent **and** systemic toxic NF **and**/**or** constituent ions **or** molecules'											
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11

function 'H-O-G2'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Secondary_Organs_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Secondary_Organs_Info(tl).epqs	X
A4	result := result + DG_Inflammation_Secondary_Organs_Info(tl).epqs	X
A5	result := result + DG_Genotoxicity_Secondary_Organs_Info(tl).epqs	X
		R1

Class 'H-O-G3' is kind of 'H-O'

H-O-G3: NFs showing gradual dissolution : Following oral exposure both NFs and constituent ions or molecules may drive antimicrobial impacts, such as reducing microbial content and diversity within the GIT.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-G3"	
lead	: String	"IIT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs showing gradual dissolution : Following oral exposure both NFs and constituent ions or molecules may drive antimicrobial impacts, such as reducing microbial content and diversity within the GIT."	
rationale	: String	"For the group of ‘gradual ’dissolving NFs (H-O-G), both the NF (potentially with reduced size) and the soluble form of the material co-exist. To be grouped as gradual dissolving the NF must exhibit a t1/2 between 2 hours and 60 hours in the OGI simulant fluids. Microbiota dysbiosis is assessed by several descriptors (i.e., PC surface properties, reactivity, cytotoxicity and barrier impairment) that can be differently analysed: for SbD/precautionary based grouping, a qualitative similarity assessment may be sufficient to assume, based on expert judgment, that the hazard (microbiota dysbiosis) is driven by not accumulating NF (itself and/or its constituent ions or molecules). On the contrary, if the grouping is made in preparation of regulation, where read-across is expected, the H-O-G3 IATA provides guidance for a quantitative similarity assessment by identifying NFs with similar chemical composition. The accompanying TTS provides a practical guidance on how to assess the ‘target ’NF versus the ‘’source. Importantly, in line with ECHA guidelines (ECHA 2019) the oral IATAs indicate that the quantitative similarity assessment must be applied to all DNs in the IATA. Here, if the NF behaves very similarly in comparison to the identified ‘’source across all DNs, the similarity assessment is considered successful and poses the conditions for performing read across following the available regulatory guidelines. If the similarity is not accepted (NF and source material are not sufficiently similar for read across), the user, for SbD and precautionary, should assume hazard (microbiota dysbiosis) is driven by NF (itself and/or its constituent ions or molecules)."	

Operators

function 'H-O-G3'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman							ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL			EXCL	MI		IRR	-
C3	likely_exposure_routes	-			-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	gradual	ELSE	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	INCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Consider hypothesis H-O-Q, H-O-S or H-O-I on quick, very slow and in-stantaneous dissolving NF"					
A3	group := 'NF dissolves gradually **in** OGI fluids'		X						
		R1	R2	R3	R4	R5	R6	R7	R8

function 'H-O-G3'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Bacterial_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Bacterial_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Bacterial_Info(tl).epqs	X
		R1

Class 'H-O-S1' is kind of 'H-O'

H-O-S1: NFs with a very slow dissolution rate: Following oral exposure NFs will maintain nanospecific activity that may lead to local inflammation within the GIT.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-S1"	
lead	: String	"IT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs with a very slow dissolution rate: Following oral exposure NFs will maintain nanospecific activity that may lead to local inflammation within the GIT."	
rationale	: String	"The 'very slow 'dissolving hypothesis considers biopersistent NFs that exhibit a t1/2 greater than 60 hours in simulant OGI juices. To be grouped as very slow dissolving NF and locally toxic, the NFs must also induce local toxicity to intestine The H-O-S1 is then accepted with the user assuming a priori as a precaution that the NF can cause local toxicity to intestine. For regulatory purpose the user should, on the contrary, consider further testing for local toxicity or read across to similar NF. If local toxicity to intestine is not found the user should consider, for SbD and precautionary measurements, a delayed local toxic response or the H-O-S2 on systemic toxicity."	

Operators

function 'H-O-S1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman							ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL			EXCL	MI		IRR	-
C3	likely_exposure_routes	-			-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	very_slow	ELSE	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	INCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Consider hypothesis H-O-I, H-O-Q or H-O-G on Instantaneous, quick or gradual dissolving NF"					
A3	group := 'NF dissolves very slow **in** OGI fluids'		X						
		R1	R2	R3	R4	R5	R6	R7	R8

function 'H-O-S1'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Intestinal_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Intestinal_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Intestinal_Info(tl).epqs	X
A5	result := result + DG_Inflammation_Intestinal_Info(tl).epqs	X
A6	result := result + DG_Genotoxicity_Intestinal_Info(tl).epqs	X
		R1

Class 'H-O-S2' is kind of 'H-O'

H-O-S2: NFs with a very slow dissolution rate: Following oral exposure NFs will maintain nanospecific activity that may drive translocation across the GIT wall, subsequent biopersistence in the body and systemic toxicity in secondary organs.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-S2"	
lead	: String	"IT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs with a very slow dissolution rate: Following oral exposure NFs will maintain nanospecific activity that may drive translocation across the GIT wall, subsequent biopersistence in the body and systemic toxicity in secondary organs."	
rationale	: String	"The ‘very slow ’dissolving hypothesis considers biopersistent NFs that exhibit a t1/2 greater than 60 hours in simulant OGI juices. To be grouped as very slow dissolving and highly biopersistent, the NFs must also exhibit a t1/2 greater than 1440 hours in lysosomal simulant fluid. Once the OGI and lysosome dissolution DNs are accepted, the IATA allows the NFs to be grouped as inducing chronic systemic toxicity and having high biopersistence (due to the potential for long-term accumulation of nanoforms in secondary organs). The H-O-S2 is then accepted with the user either assuming a priori as a precaution that the NF can cause chronic toxicity in secondary organs or considering further targeted testing. In the case of a regulatory purpose, a read across from NFs of similar composition is suggested. If the NF presents a dissolution half-life faster than 1440 hours in simulant lysosomal fluid, the user rejects the hypothesis, but stringent precautionary measures can still be undertaken."	

Operators

function 'H-O-S2'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman											ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL							EXCL	MI		IRR	-
C3	likely_exposure_routes	-							-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	very_slow					ELSE	-	-	-	-	-
C5	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	?	very_slow		ELSE		-	-	-	-	-	-
C6	purpose	-	-	'precaution-ary', 'safe-by-design'	ELSE	'precautionary', 'safe-by-design'	ELSE	-	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	MI	INCL	INCL	EXCL	EXCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)					"NF will not be highly biopersistant; possible toxicity from released ions or molecules."	"NF will not be highly biopersistant; possible toxicity from released ions or molecules."	"Consider hypothesis H-O-I, H-O-Q or H-O-G on Instantaneous, quick or gradual dissolving NF."					
A3	consequences→Add(#)					"No systemic toxicity is expected due to bi-opersistence. Consider possible chronic sys-temic toxicity."	"No systemic toxicity is expected due to biopersistence."						
A4	group := 'Highly biopersistent NF **and** chronic systemic toxic'			X									
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12

function 'H-O-S2'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Secondary_Organs_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Secondary_Organs_Info(tl).epqs	X
A4	result := result + DG_Inflammation_Secondary_Organs_Info(tl).epqs	X
A5	result := result + DG_Genotoxicity_Secondary_Organs_Info(tl).epqs	X
		R1

Class 'H-O-S3' is kind of 'H-O'

H-O-S3: NFs with a very slow dissolution rate : Following oral exposure NFs will maintain nanospecific activity that will drive antimicrobial impacts, such as reducing microbial content and diversity within the GIT

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-O-S3"	
lead	: String	"IT/RIVM (Luisana, Stefania/Susan)"	
description	: String	"NFs with a very slow dissolution rate : Following oral exposure NFs will maintain nanospecific activity that will drive antimicrobial impacts, such as reducing microbial content and diversity within the GIT"	
rationale	: String	"The 'very slow 'dissolving hypothesis considers biopersistent NFs that exhibit a t1/2 greater than 60 hours in simulant OGI juices. To be grouped as very slow dissolving NF and as microbiota dysbiosis inducer, the NFs must also drive antimicrobial impacts. The H-O-S3 is then accepted with the user assuming a priori as a precaution that the NF could reduce microbial content and diversity within the intestine. For regulatory purpose the user should, on the contrary, subsequent microbiome dysbiosis after repeated oral exposure. If microbiota dysbiosis is not found the user should consider, for SbD and precautionary measurements, the H-O-S1 and H-O-S2 on local or systemic toxicity."	

Operators

function 'H-O-S3'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stHuman							ELSE
C2	NF_exposure_to_human_GI_tract_likely()	INCL			EXCL	MI		IRR	-
C3	likely_exposure_routes	-			-	oral	ELSE	-	-
C4	targ_NF.DN_dissolution_outcome_in_GI_fluids	?	very_slow	ELSE	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	MI	INCL	EXCL	IRR	MI	IRR	IRR	IRR
A2	consequences→Add(#)			"Consider hypothesis H-O-I, H-O-Q or H-O-G on Instantaneous, quick or gradual dissolving NF"					
A3	group := 'NF dissolves very slow **in** OGI fluids'		X						
		R1	R2	R3	R4	R5	R6	R7	R8

function 'H-O-S3'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_GIF_Info(tl).epqs	X
A2	result := result + DG_Reactivity_Bacterial_Info(tl).epqs	X
A3	result := result + DG_Cytotoxicity_Bacterial_Info(tl).epqs	X
A4	result := result + DG_BarrierIntegrity_Bacterial_Info(tl).epqs	X
		R1

Class 'H-D' is kind of HumanHypothesis

Well defined dermal hypothesis classes.

Operators

function 'H-D'::DN_Dissolution_SW_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	/* H-D-1, H-D-2, H-D-3, H-D-4 */		
A2	result := DN_Info→**New**	X	X
A3	result.intro	"In vitro dissolution assay in sweat fluids."	
A4	result.preferred_methods	"static or dynamic (ISO/TR 19057:2017) dissolution using relevant sweat simulant fluids"	
A5	result.guidance_for_assay_selection	"NF dissolution should be assessed in physiologically relevant simulated sweat fluid using a static or dynamic set-up depending on both media composition and model system requirements. different recipes to prepare simulated sweat are available. These mainly differ in pH and in the presence of amino acids, however both these factors potentially influence NF dissolution. For this reason, as the range of sweat pH normally vary from acid to basic condition (Bandodkar et al 2013), we recommend the use of simulant sweat fluids that include representative amino acids of human sweat and to apply a basic and an acidic pH (i.e. pH 5 and pH 8)."	
A6	result.tier_escalation	"Tier 1 provides sufficient evidence for grouping a NF as instantaneously dissolving NF in simulated sweat fluids."	
A7	/* Screening batch or continuous flow system ISO 19057:2017 */	X	
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, 'Simulated sweat')))	X	
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Simulated sweat')))	X	
A10	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Simulated sweat')))	X	
		R1	R2

function 'H-D'::DN_Inorganic_or_non_flexible_organic_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"[basic info] Chemical composition (main chemicals, user knowledge)"	
		R1	R2

function 'H-D'::DN_constituent_particle_diameter_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Constituent particle size distribution"	
A3	result.preferred_methods	"TEM (ISO/PRF 21363), AFM (ISO 13095:2014), XRD (ISO/TS 80004-6:2021)"	
A4	result.guidance_for_assay_selection	"Assay selection is based on user expertise."	
A5	/* TEM ISO/PRF 21363, AFM ISO 13095:2014, XRD ISO/TS 80004-6:2021 */	X	
A6	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Sterile filtered water'), slConstituentParticleLevel)))	X	
A7	result.epqs→Add(WTG(ENUM(EPQM(PC_GRANULOMETRY::EP_DnPx_D1, 'Simulated sweat'), slConstituentParticleLevel)))	X	
		R1	R2

function 'H-D'::DG_aggregated_size_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Size analysis on NF agglomerates/ aggregates."	
A3	result.preferred_methods	"DLS (ISO/TS 80004-6:2015 3.2.7), NTA (ISO/TS 80004-6:2015 3.2.8)"	
A4	result.guidance_for_assay_selection	"Assay selection is based on user expertise."	
A5	/* DLS ISO/TS 80004-6:2015 3.2.7), NTA, ISO/TS 80004-6:2015 3.2.7 */		
A6	result.epqs→Add(WTG(EPQM(PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER, 'Sterile filtered water')))	X	
A7	result.epqs→Add(WTG(EPQM(PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER, 'Simulated sweat')))	X	
		R1	R2

function 'H-D'::DG_Hydrophobicity_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Hydrophobicity"	
A3	result.preferred_methods	"Surface contact angle determination (Nanoscale, 11, 17637-17654, 2019)"	
A4	result.guidance_for_assay_selection	"Surface contact angle to water can be used as a descriptor of nanomaterial hydrophobicity, with θ <90° considered hydrophilic and θ >90° considered hydrophobic. At the moment as no standardized methods are available to test the hydrophobicity, we suggest in the to follow the surface contact angle determination method in Wohlleben et al. (Wohlleben et al., 2019)."	
A5	/* Water contact angle */	X	
A6	result.epqs→Add(WTG(EPQM(PC_SURFACE_TENSION::EP_WATER_CONTACT_ANGLE, 'Sterile filtered water')))	X	
		R1	R2

function 'H-D'::DG_Reactivity_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Acellular ROS measurements"	
A3	result.preferred_methods	"DCFH2-DA (GRACIOUS SOP), EPR (ISO 18827), FRAS (GRACIOUS SOP)"	
A4	result.guidance_for_assay_selection	"Surface reactivity is expected to be a main determinant of the toxicity of nanoforms. Highly reactive nanoforms might induce irritation reactions. Although a specific sensitizing response to nanoforms is rather unlikely, they could behave as coadjuvants, exacerbating the sensitizing responses to other sensitizers. Surface reactivity could be addressed by acellular reactivity assays, such as the 2',7'-dichlorodihydrofluorescein diacetate (DCFH2-DA) following the GRACIOUS SOP, the electron Paramagnetic Resonance (EPR) following the ISO 18827, and the ferric reducing ability of serum assay (FRAS) following Gandon et al. (Gandon et al., 2017). The use of a combination of assays for regulatory implications is recommended."	
A5	/* EPR, ISO TS 18827(ISO 2017) */	X	
A6	result.epqs→Add(WTD(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY)))	X	
A7	/* FRAS, SOP in D5.3 of GRACIOUS */	X	
A8	result.epqs→Add(WTD(EPQM(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE, 'Human blood serum (HBS)')))	X	
A9	result.epqs→Add(WTD(EPQM(PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE, 'Human blood serum (HBS)')))	X	
A10	/*DCFH-DA, SOP in D5.3 of GRACIOUS */	X	
A11	result.epqs→Add(WTD(OP(EPQ(PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU), oPEAK)))	X	
		R1	R2

Class 'H-D-1' is kind of 'H-D'

Hypothesis H-D-1: NFs with an instantaneous dissolution: Following dermal exposure NFs will dissolve into their molecular or ionic form before they reach the viable layers of the skin and will cause similar toxicity as substances instantaneoulsy releasing, dissolving and/or transforming into the same ionic or molecular forms.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-D-1"	
lead	: String	"LEITAT/RIVM/BfR"	
description	: String	"NFs with an instantaneous dissolution: Following dermal exposure NFs will dissolve into their molecular or ionic form before they reach the viable layers of the skin and will cause similar toxicity as substances quickly releasing, dissolving and/or transforming into the same ionic or molecular forms."	
rationale	: String	"H-D-1: NFs with an instantaneous dissolution: Following dermal exposure the NFs will dissolve into their molecular or ionic form before they reach the viable layers of the skin and will cause similar toxicity as substances instantaneously releasing, dissolving and/or transforming into the same ionic or molecular forms. The main purpose of hypotheses H-D-1 is to exclude particle specific toxicity and therefore group (and perform read-across to the toxicity profile from CLP classification and DNELs by dermal route) with other substances instantaneously releasing/transforming into the same ionic or molecular forms. The implications are to assume the same CLP classification and dermal DNELs for the NF compared to the source materials (i.e. substance instantaneously releasing the same ionic or molecular forms)."	

Operators

function 'H-D-1'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman						ELSE
C2	targ_NF	nil	ELSE					-
C3	likely_exposure_routes	-	0	dermal			ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_sweat_fluid	-	-	?	instantaneously	ELSE	-	-
C5	purpose	-	-	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	INCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"NFs can be grouped as instantaneously dissolving. No particle specific toxicity is expected."	"Dermal exposure of viable layers of the skin to particles possible. Consider hypotheses H-D-2, H-D-3, H-D-4 and H-D-5"		
A3	consequences→Add(#)				"Perform read-across to source material releasing the same molecular or ionic form for dermal irritation, sensitization."			
		R1	R2	R3	R4	R5	R6	R7

function 'H-D-1'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_SW_Info(tl).epqs	X
		R1

Class 'H-D-2' is kind of 'H-D'

Hypothesis H-D-2: Non flexible NFs will not penetrate (in their particle form) to viable layers of the skin above 1% of the applied dose.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-D-2"	
lead	: String	"LEITAT/RIVM/BfR"	
description	: String	"NFs that are not flexible, following dermal exposure will result in limited or no dermal absorption."	
rationale	: String	"The main purpose of these hypotheses is to group the NFs that will only penetrate the skin in limited amounts (1% of the applied dose can be used as worst-case estimate). If dermal absorption data of a source material with similar chemical composition and surface properties is available, read-across for systemic absorption data and any toxicity related to dermal exposure can be performed to this source material when this only differs in size to the target material. The main decision nodes in this IATA imply dissolution in sweat (to exclude quickly soluble materials for which particle-specific effects are not of concern), chemical composition and rigidity in the case of organic particles (to exclude particles which size/conformation could change), and particle size. Regarding size, constituent particle size is sufficient to conclude that a worst-case absorption threshold is applicable. However, in order to conclude on the applicability of read-across for absorption data or toxicity to a source material, the aggregated size should also be available."	

Operators

function 'H-D-2'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman										ELSE	
C2	targ_NF	nil	ELSE									-	
C3	likely_exposure_routes	-	0	dermal							ELSE	-	
C4	targ_NF.DN_dissolution_outcome_in_sweat_fluid	-	-	?	gradual, very_slow					ELSE		-	-
C5	targ_NF.DN_is_inorganic_or_non_flexible_organic	-	-	-	?	Yes			No	-		-	-
C6	source_material	-	-	-	-	nil	ELSE		-	-		-	-
C7	purpose	-	-	-	-	-	'regulatory'	ELSE	-	-		-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	EXCL	INCL	INCL	EXCL	EXCL		IRR	IRR
A2	consequences→Add(#)					"Assume relevant exposure of the viable epidermis and dermis, as well as systemic exposure to NP may occur."	"Read across dermal absorption and/or toxicity data (i.e. CLP for irritation, sensitization and DNEL dermal) to source material."		"Assume relevant exposure of the viable epidermis and dermis, as well as systemic exposure to NP may occur."	"No particle specific toxicity is expected. Consider hypotheses H-D-1 and H-D-2"			
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	

function 'H-D-2'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_SW_Info(tl).epqs	X
A2	result := result + DN_Inorganic_or_non_flexible_organic_Info(tl).epqs	X
A3	result := result + DN_constituent_particle_diameter_Info(tl).epqs	X
A4	result := result + DG_aggregated_size_Info(tl).epqs	X
A5	result := result + DG_Hydrophobicity_Info(tl).epqs	X
A6	result := result + DG_Reactivity_Info(tl).epqs	X
		R1

Class 'H-D-3' is kind of 'H-D'

Hypothesis H-D-3: Non flexible NFs > 5 nm will not penetrate (in their particle form) to viable layers of the skin above 1% of the applied dose.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-D-3"	
lead	: String	"LEITAT/RIVM/BfR"	
description	: String	"NFs that are not flexible and larger than 5 nm, following dermal will result in limited or no dermal absorption."	

Operators

function 'H-D-3'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman											ELSE	
C2	targ_NF	nil	ELSE										-	
C3	likely_exposure_routes	-	0	dermal								ELSE	-	
C4	targ_NF.DN_dissolution_outcome_in_sweat_fluid	-	-	?	gradual, very_slow						ELSE	-	-	
C5	targ_NF.DN_is_inorganic_or_non_flexible_organic	-	-	-	?	Yes				No	-	-	-	
C6	source_material	-	-	-	-	nil			ELSE	-	-	-	-	
C7	targ_NF.DN_constituent_particle_diameter_exceeds_5nm	-	-	-	-	?	Yes		No	-	-	-	-	
C8	purpose	-	-	-	-	-	'regulatory'	ELSE	-	-	-	-	-	
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	INCL	INCL	EXCL	EXCL	EXCL	EXCL	IRR	IRR
A2	consequences→Add(#)						"Dermal penetration (healthy skin) expected to be minimal (<1%) under normal conditions. Repeated long-term exposures and scenarios with damaged skin, may require specific assessments."				"Assume relevant exposure of the viable epidermis and dermis, as well as systemic exposure to NP may occur."	"No particle specific toxicity is expected. Consider hypotheses H-D-1 and H-D-2"		
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13

function 'H-D-3'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_SW_Info(tl).epqs	X
A2	result := result + DN_Inorganic_or_non_flexible_organic_Info(tl).epqs	X
A3	result := result + DN_constituent_particle_diameter_Info(tl).epqs	X
A4	result := result + DG_aggregated_size_Info(tl).epqs	X
A5	result := result + DG_Hydrophobicity_Info(tl).epqs	X
A6	result := result + DG_Reactivity_Info(tl).epqs	X
		R1

Class 'H-D-4' is kind of 'H-D'

Hypothesis H-D-4: NFs that are not biopersistent: Dermal exposure to NFs will not lead to accumulation of NFs or subsequent systemic toxicity.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-D-4"	
lead	: String	"LEITAT/RIVM/BfR"	
description	: String	"NFs that are not biopersistent: Dermal exposure to NFs will not lead to accumulation of NFs or subsequent systemic toxicity."	
rationale	: String	"The main purpose of this hypothesis is to exclude systemic toxicity associated with the accumulation of particles, as non-biopersistent NFs will quickly dissolve in the biological fluid. Therefore, the main decision node in this IATA is the dissolution half-life in lysosomal fluid. If this half-life is below 48 hours, it is concluded that there are no concerns on systemic accumulation of particles. In the case of a SbD or screening context, considering also the generally low absorption rate of particles, the conclusion would be to waive any concerns on particle-specific toxicity by the dermal route."	

Operators

function 'H-D-4'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman								ELSE
C2	targ_NF	nil	ELSE							-
C3	likely_exposure_routes	-	0	dermal					ELSE	-
C4	targ_NF.DN_dissolution_outcome_in_lysosomal_fluid	-	-	?	quick	ELSE			-	-
C5	purpose	-	-	-	-	'safe-by-design'	'regulatory'	ELSE	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	MI	INCL	EXCL	EXCL	EXCL	IRR	IRR

A2	consequences→Add(#)				"Group as non-biopersistent NF"					
A3	consequences→Add(#)				"Assume NF will not lead to particle-specific systemic toxicity due to accumulation"	"There may be some concern for accumulation and related toxicity, but rather unlikely and issue due to low expected absorption."	"Consider further testing to evaluate absorption and/or toxicity."			
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'H-D-4'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_SW_Info(tl).epqs	X
		R1

Class 'H-D-5' is kind of 'H-D'

Hypothesis H-D-5: NFs with constituent substance(s) or degradation products classified for dermal irritation or sensitization: Dermal exposure to NFs may result in dermal irritation or sensitization.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis H-D-5"	
lead	: String	"LEITAT/RIVM/BfR"	
description	: String	"NFs with constituent substance(s) or degradation products classified for dermal irritation or sensitization: Dermal exposure to NFs may result in dermal irritation or sensitization."	
rationale	: String	"The main purpose of this hypothesis is to conclude whether the presence of chemical components with CLP classifications for dermal irritation/sensitization should lead to the same CLP classification for the NFs. Even in cases where the chemical content is above thresholds for classification of mixtures, the NF may not need to be classified if the percentage of dissolution of such chemical components is not above such thresholds over a worst-case residence period (preliminarily fixed at 72 hours). Therefore, measuring dissolution is a critical decision node for grouping within this IATA. Although 8 to 24 hours are most commonly used values for residence of chemicals in skin, in the case of particles, these may accumulate in hair follicles leading to longer residence times. The implications are to assume the same CLP classification for the NF compared to the source materials (i.e. chemical components of the NF that are classified for dermal irritation/sensitization)."	

Operators

function 'H-D-5'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stHuman												ELSE	
C2	targ_NF	nil	ELSE											-	
C3	likely_exposure_routes	-	0	dermal									ELSE	-	
C4	targ_NF.DN_NF_contains_or_degrades_to_CLP_classified_substances	-	-	?	Yes							No		-	-
C5	purpose	-	-	-	'regulatory'						ELSE	-		-	-
C6	targ_NF.DN_classified_substances_content_above_thresholds_for_classification_of_mixtures	-	-	-	?	Yes				No	-	-		-	-
C7	targ_NF.DN_dissolved_fraction_classified_substances_in_sweat_fluid_above_thresholds_for_classification_of_mixtures	-	-	-	-	?	Yes		No	-	-	-		-	-
C8	purpose	-	-	-	-	-	-		-	-	-	'safe-by-design'	ELSE	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	INCL		EXCL	EXCL	INCL	EXCL	EXCL	IRR	IRR
A2	consequences→Add(#)						"Regulatory read-across: Assume NF will cause dermal irritation or sensitization: Read-across to classified source material for the hazard classification for skin irritation or sensitization."		"Consider further testing for irritation and sensitization to exclude potential 'particle-effects' due to physical effects or surface reactivity (OECD TGs and IATAs for dermal irritation and sensitization)."	"Consider further testing for irritation and sensitization to exclude potential 'particle-effects' due to physical effects or surface reactivity (OECD TGs and IATAs for dermal irritation and sensitization)."	"Assume dermal exposure may result in dermal irritation or sensitization."	"If data exist and are negative, assume no dermal irritation or sensitization."	"If no data exist, consider further testing (OECD TGs and IATAs for dermal irritation and sensitization)."		
		R1	R2	R3	R4	R5	R6		R7	R8	R9	R10	R11	R12	R13

function 'H-D-5'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_SW_Info(tl).epqs	X
		R1

Class `EnvHypothesis` is kind of `Hypothesis`

Well defined hypothesis classes on Environmental fate

Class `'E-G'` is kind of `EnvHypothesis`

Well defined hypothesis classes on Environmental fate

Class `'E-G-1'` is kind of `'E-G'`

Hypothesis E-G-1

Defined expressions

name	type	expression	comment
rationale	: String	"Environmental toxicity in aquatic systems Either ions (in E-G-1a) or particles (in E-G-1b and E-G-1c) are assumed to be the sole contributors to toxicity in the extreme cases, independent of their inherent toxicity. In addition (in E-G-1d), there is also the possibility of ions or particles being the main contributors to toxicity in case of a very high or very low ratio of ion:particle toxicity. In the case of a very high ratio of ion:particle toxicity, ions are the dominant contributor to toxicity, whereas the opposite is true in case of a very low ratio. Again, at this moment fixed cut-off values for identifying ‘very ’high and ‘very ’low have not yet been defined. Instead, preliminary estimates are provided. It is to be noted that in common practise, excess ion toxicity is the rule rather than the exception for most NFs. In between the four extreme scenarios depicted above, various combinations of dissolution rate constants and ion:particle toxicity ratios are possible. The toxicity of a suspension of particles and ions can be described as a multi-dimensional plane that, at a fixed exposure time, is spanned by the dissolution rate constant and the ion:particle toxicity ratio."	

Operators

function 'E-G-1'::DN_Dissolution_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* Do NFs dissolve in the relevant medium / media? E-G-1a,b,c,d,e,f */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Screening tests to assess if NFs dissolve in simple media."	"Extended tests to assess if NFs dissolve in simple media."	"Extended tests to assess if NFs dissolve in environmentally/biologically relevant medium/ media."	
A4	result.preferred_methods	"Screening batch dissolution test (OECD GD 318)"	"Extended batch dissolution test (OECD GD 318), Extended continuous flow system dissolution test (ISO TR 19057:2017)"		
A5	result.guidance_for_assay_selection	"When assessing the dissolution rate of nanoforms in the environment, quickly dissolving materials may be identified through simple screening using a batch dissolution test based on the methodology from OECD 29, with adaptations for nano-specific considerations detailed in OECD GD 318. NFs which pass the threshold for “fully dissolved” in all three pH media in this screening assessment may be considered quickly dissolving and require no further nano-specific testing for dissolution their dissolution rate."	"Nanoforms which are not considered quickly dissolving can be assessed using either a batch or continuous flow system in an extended dissolution test. Measurements at intervals across the test duration allows calculation of the dissolution rate expressed as a function of surface area of the NF, using the Noyes-Whitney equation (OECD GD 318). Based on the results from the Tier 1 screening batch dissolution test, the most appropriate Tier 2 test may be selected. From existing knowledge, exact cut-offs for when batch versus continuous flow system dissolution testing are not possible to define. However, current experiences indicate materials with a solubility between 1 and 10 mgL-1 may be better suited to testing with the continuous flow system (ISO TR 19057:2017), whilst materials with a solubility <1 mgL-1 may be better tested using the extended batch dissolution test (OECD GD 318). "	"The same considerations apply for choosing between batch and continuous flow systems as for Tier 2 testing. However, the choice of relevant environmental or biological media and the relevant test duration must be driven by the specific purpose of the grouping. More details on how to select relevant test durations and starting concentrations can be found in the OECD Guidance Document 318."	
A6	result.tier_escalation	"NFs that pass the threshold for quickly dissolving in the screening batch dissolution test need not progress to tier 2 testing. Passing ≥ 90% dissolution at pH 5, 7 and 9 in 24 hours with a starting concentration of 10 mgL-1 is considered to represent sufficiently fast dissolution for all relevant mass of the NF to be in the dissolved fraction in the environment (OECD GD318). Therefore, no high tier testing is required for these NFs. For those which do not pass this threshold in the tier 1 screening batch dissolution test, progression to the extended dissolution test in tier 2 may be necessary."	"Tier 2 extended dissolution testing delivers an understanding of the dissolution rate of the NF in relation to a sole independent variable, pH. Escalation to Tier 3 testing in environmentally or biologically relevant media is recommended if there is specific cause for demonstrating dissolution rates within a particular media, for example if the user requires demonstration of similar behavior within the exposure conditions of a particular in vivo ecotoxicity test."		
A7	/* Batch dissolution test, ISO 19057:2017 */				
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 5')))	X			X
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 7')))	X			X
A10	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 9')))	X			X
A11	/* Continuous flow system,ISO 19057:2017 */				
A12	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 4')))		X		X
A13	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 7')))		X		X
A14	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 9')))		X		X
A15	/* Continuous flow system in relevant aquatic test medium, ISO 19057:2017 */				
A16	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Relevant aquatic medium')))			X	X
		R1	R2	R3	R4

function 'E-G-1'::DN_Dispersion_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	/* Do particles form a stable dispersion in the relevant medium / media? */				
A2	result := DN_Info→**New**	X	X	X	X
A3	result.intro	"Screening dispersion test (6h, +NOM, 3 pH levels, 3 Ca(NO3)2 levels) according to OECD TG 318."	"Extended dispersion test (6h, +/- NOM, 3 pH levels, 3 Ca(NO3)2 levels) according to OECD TG 318."	"Extended dispersion test (6h, in relevant medium, e.g. test medium to be used for toxicity test, specific surface water(s)) according to OECD TG 318."	
A4	result.preferred_methods	"Screening dispersion test (OECD TG 318)"	"Extended dispersion test (OECD TG 318)"	"Screening dispersion test - heteroaggregation (Adapted OECD TG 318, based on OECD GD 318), Extended dispersion test in environmentally relevant medium/ media (OECD TG 318), Nanomaterial removal in wastewater (OECD WNT 3.11)"	
A5	result.guidance_for_assay_selection	"When assessing dispersion stability, the screening test assesses a matrix of 3 ionic strengths and 3 pH all with a fixed concentration of NOM, considered representative of the majority of surface waters (OECD TG 318). This allows for identification of high stability and low stability NFs after measurement at a single time point without the need for extended dynamic testing across time."	"The extended dispersion stability test (OECD TG 318)."		
A6	result.tier_escalation	"NFs that pass the threshold for high dispersion stability (≥90% of the material remains in dispersion under all tested conditions in the screening dispersion stability test) need not escalate to Tier 2 extended dispersion stability testing. These NFs are considered to form a stable dispersion. NFs that pass the threshold for low dispersion stability (≤10% of the material remains in dispersion under all tested conditions in the screening dispersion stability test) need not escalate to Tier 2 extended dispersion stability testing. These NFs are considered unstable. NFs for which different amounts of material are left in dispersion in different conditions after the 6 hour screening dispersion test are considered partially stable, and must be tested in Tier 2 extended dispersion stability test to further refine the decision and to allow for similarity assessment of dispersion stability for partially stable NFs."	"Escalation to Tier 3 is may not be as a result of outcomes from Tier 2 testing. Rather the use of Tier 3 testing either of the screening dispersion test for heteroaggregation (Adapted OECD TG 318, based on OECD GD 318) or the extended dispersion test (OECD TG318) but in relevant test medium/ surface water should be driven by the purpose of the grouping and the users judgment."		
A7	/* Screening dispersion test + Extended dispersion test, OECD TG 318 */				
A8	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)')))	X	X		
A9	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)')))	X	X		
A10	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)')))	X	X		
A11	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 4)')))		X		
A12	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 7)')))		X		
A13	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 9)')))		X		
A14	/* Screening dispersion test - heteroaggregation, Adapted OECD TG 318 (based on OECD GD 318) */				
A15	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 alternative media/test media + NOM (0, 1, 10 Ca(NO3)2, pH 4, 7, 9) + SPM')))			X	
A16	/* Extended dispersion test, OECD TG 318 */				
A17	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'Relevant aquatic medium')))			X	
		R1	R2	R3	R4

function 'E-G-1'::DN_Density_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro				
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection				
A5	result.epqs→Add(WTG(EPQ(PC_DENSITY::EP_SKELETAL_DENSITY)))	X			
		R1	R2	R3	R4

function 'E-G-1'::DN_ToxicityRatio_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Standard acute aquatic toxicity tests according to OECD or ISO guidelines. Suited test organisms, amongst others: algae, daphnid, fish."	"Advanced aquatic toxicity tests according to OECD or ISO guidelines, focusing on additional organisms and/or additional endpoints of acute toxicity."	"Advanced aquatic toxicity tests according to OECD or ISO guidelines, focusing on additional organisms and/or chronic toxicity endpoints."	
A3	result.preferred_methods	"Freshwater Alga and Cyanobacteria, Growth Inhibition Test (OECD GD 201), or: Daphnia sp., Acute Immobilisation Test (OECD GD 202), or: Fish, Early-life Stage Toxicity Test (OECD GD 210), or: Fish, Acute toxicity test with embryos (OECD GD 236), or: Daphnia magna Reproduction Test (OECD TG 211)."	"Chironomus sp., Acute Immobilisation Test (OECD 235), or: Fish, Acute Toxicity Testing (OECD GD 203), or: Lemna sp. Growth Inhibition Test (OECD GD 221)."	"Fish Short Term Reproduction Assay (OECD 229), or: 21-day Fish Assay - A Short-Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition (OECD GD 230)."	
A4	result.guidance_for_assay_selection	"Testing is performed with suspensions of the NF and with the solute. Preferably more than one assay is selected, there is on forehand no preference for selection of any of the assays indicated. If the resulting EC50 or LC50 values differ by more than one order of magnitude, it can be assumed that either the NF or the solute contributes most to toxicity. The full dose-response curve is used to quantify the contributions of NF and solute to suspension toxicity. Any of the other tier 1-tests may be performed to confirm the differences in toxicity between NF and solute and the contributions to toxicity of NF and solute."	"Longer-term testing is performed with NF suspensions. Similar to Tier 1 the focus is on quantifying the contributions of NF and solute to suspension toxicity. Preferably more than one Tier 2 test is selected for this purpose."	"Longer-term testing is performed with NF suspensions, focusing on additional endpoints. Similar to Tier 1 the focus is on quantifying the contributions of NF and solute to suspension toxicity."	
A5	result.tier_escalation	"NFs for which the ratio of LC50- or EC50-values of NF and solute is in between 0.1 and 10 progress to tier 2 testing. When detailed dose-response information is available, this is also the case for the NFs for which the contribution to toxicity of either NF or solute is in between 10 and 90 % at any exposure concentration."	"Tier 3 extended toxicity testing is focused on chronic endpoints. Tier 3 testing is performed to confirm the contributions of NF and solute to suspension toxicity."		
A6	/* Freshwater Alga and Cyanobacteria, Growth Inhibition Test OECD TG 201 */	X			
A7	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_ALGAE_TOX::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%)))	X			
A8	/* Daphnia sp., Acute Immobilisation Test, OECD TG 202 */	X			
A9	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_AQUATIC_INVERT_TOX_SHORT::EP_MORTALITY, ·mg·l^{-1}), LC_x), 50.0·%)))	X			
A10	/* Fish, Early-life Stage Toxicity Test */	X			
A11	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_CHRONIC::EP_HATCHING, ·mg·l^{-1}), EC_x), 50.0·%)))	X			
A12	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_CHRONIC::EP_HATCHING, ·mg·l^{-1}), LC_x), 50.0·%)))	X			
A13	/* Acute toxicity test with fish embryos, OECD TG 236 */	X			
A14	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_SHORT::EP_MORTALITY, ·mg·l^{-1}), EC_x), 50.0·%)))	X			
A15	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_SHORT::EP_MORTALITY, ·mg·l^{-1}), LC_x), 50.0·%)))	X			
A16	/* Daphnia magna Reproduction Test */	X			
A17	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_AQUATIC_INVERT_TOX_CHRONIC::EP_IMMOBILIZATION, ·mg·l^{-1}), EC_x), 50.0·%)))	X			
A18	/* Chironomus sp., Acute Immobilisation Test, OECD TG 235 */		X		
A19	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_AQUATIC_INVERT_TOX_SHORT::EP_GROWTH, ·mg·l^{-1}), LC_x), 50.0·%)))		X		
A20	/* Fish, Acute Toxicity Testing, OECD TG 203 */		X		
A21	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_SHORT::EP_MORTALITY, ·mg·l^{-1}), EC_x), 50.0·%)))		X		
A22	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_SHORT::EP_MORTALITY, ·mg·l^{-1}), LC_x), 50.0·%)))		X		
A23	/* Lemna sp. Growth Inhibition Test, OECD TG 221 */		X		
A24	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_AQ_PLANTS_NONE_ALGAE::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%)))		X		
A25	/* Fish Short Term Reproduction Assay, OECD TG 229 */			X	
A26	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_CHRONIC::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%)))			X	
A27	/* 21-day Fish Assay - A Short-Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition, OECD TG 230 */			X	
A28	result.epqs→Add(WTD(PER(ENUM(EPQU(EC_FISH_TOX_CHRONIC::EP_MORTALITY, ·mg·l^{-1}), EC_x), 50.0·%)))			X	
		R1	R2	R3	R4

Class 'E-G-1a' is kind of 'E-G-1'

Hypothesis E-G-1a: NFs with a quick dissolution rate in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the solutes.

Defined expressions

name	type	expression	comment
title	: String	"E-G-1a"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs with a quick dissolution rate in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the solutes."	

Operators

function 'E-G-1a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment							ELSE
C2	targ_NF	nil	ELSE						-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE					-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	quick			ELSE	-
C5	medium_interaction.DN_solutes_remain_their_form	-	-	-	?	Yes	No	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	INCL	EXCL	EXCL	IRR
A2	consequences→Add(#)					"Perform read-across for aquatic toxicity to similar solutes."	"Characterise/model the transformation process(es) and assess the 'new' NFs"	"Consider hypotheses E-G-1b..d on NF exposure in aquatic environments."	
A3	group					'NF aquatic toxicity is driven by the fate and toxicity characteristics of the solutes'			
		R1	R2	R3	R4	R5	R6	R7	R8

function 'E-G-1a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Dissolution_Info(tl).epqs	X	X	X	X
		R1	R2	R3	R4

Class 'E-G-1b' is kind of 'E-G-1'

Hypothesis E-G-1b: NFs with a very slow dissolution rate and a stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the NFs in aqueous environment.

Defined expressions

name	type	expression	comment
title	: String	"E-G-1b"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs with a very slow dissolution rate and a stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the NFs in aqueous environment."	

Operators

function 'E-G-1b'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment									ELSE
C2	targ_NF	nil	ELSE								-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE							-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow				ELSE		-
C5	medium_interaction.DN_dispersion_stability_in_medium_outcome	-	-	-	?	stable		ELSE	-		-
C6	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	?	Yes	No	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	INCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)						"Perform read-across for aquatic toxicity to a similar NF."	"Characterise/model the transformation process(es) and assess the 'new' NFs"	"Consider hypotheses E-G-1c on (partially) unstable dispersions."	"Consider hypotheses E-G-1a,d on (partially) dissolving NFs."	
A3	group						'NF aquatic toxicity is driven by the fate and toxicity characteristics of the NF in aquous environment'				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

function 'E-G-1b'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_Dispersion_Info(tl).epqs	X
		R1

Class 'E-G-1c' is kind of 'E-G-1'

Hypothesis E-G-1c: NFs with a very slow dissolution rate and a partial stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the NFs remaining in aqueous environments.

Defined expressions

name	type	expression	comment
title	: String	"E-G-1c"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs with a very slow dissolution rate and a partial stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of the NFs remaining in aqueous environments."	

Operators

function 'E-G-1c'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment											ELSE
C2	targ_NF	nil	ELSE										-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE									-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow							ELSE	-
C5	medium_interaction.DN_dispersion_stability_in_medium_outcome	-	-	-	?	intermediate					ELSE	-	-
C6	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	?	Yes			No	-	-	-
C7	targ_NF.density | density	-	-	-	-	-	?	density < 1.0·g·cm⁻³	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	INCL	EXCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)							"Perform read-across for aquatic toxicity to a similar NF."	"Consider hypotheses: E-WS-1a-b on NFs in sediment."	"Character-ise/model the transformation process(es) and assess the 'new' NFs"	"Consider hypo-theses E-G-1b on stable disper-sions."	"Consider hypotheses E-G-1a,d on (partially) dissolving NFs."	
A3	group												
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12

function 'E-G-1c'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_Dispersion_Info(tl).epqs	X
A3	result := result + DN_Density_Info(tl).epqs	X
		R1

Class 'E-G-1d' is kind of 'E-G-1'

Hypothesis E-G-1d: NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (a high toxicity ratio solute : NF allows read-across to similar solutes).

Defined expressions

name	type	expression	comment
title	: String	"E-G-1d"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (a high toxicity ratio solute : NF allows read-across to similar solutes)."	

Operators

function 'E-G-1d'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment															ELSE
C2	targ_NF	nil	ELSE														-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE													-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	gradual											ELSE	-
C5	medium_interaction.DN_dispersion_stability_in_medium_outcome	-	-	-	?	stable, intermediate									ELSE	-	-
C6	medium_interaction.DN_solutes_remain_their_form	-	-	-	-	?	Yes							No	-	-	-
C7	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	-	?	Yes					No	-	-	-	-
C8	targ_NF.density | density	-	-	-	-	-	-	?	density ≤ 1.0·g·cm⁻³		ELSE	-	-	-	-	-	-
C9	medium_interaction.DN_toxicity_ratio_ion_mol_vs_NF	-	-	-	-	-	-	-	?	high_ratio	ELSE	-	-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	MI	MI	INCL	EXCL	EXCL	EXCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)									"Lethal and sub-lethal toxicity to representative aquatic species is dominated by the solutes. Perform read-across to similar solutes. "	"Consider hypotheses E-G-1e-f on other toxicity ratios"	"Consider hypotheses E-WS-1a-e on NFs in sediment."	"Characterise/ model the transformation process(es) and assess the “new” NFs."	"Characterise/ model the transformation process(es) and assess the “new” NFs."	"Consider hypotheses W-S-1a-e on NFs in sediment."	"Consider hypotheses E-G-1a-c."	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16

function 'E-G-1d'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_Dispersion_Info(tl).epqs	X
A3	result := result + DN_Density_Info(tl).epqs	X
A4	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-G-1e' is kind of 'E-G-1'

Hypothesis E-G-1e: NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (a low toxicity ratio solute : NF allows read-across to similar NFs).

Defined expressions

name	type	expression	comment
title	: String	"E-G-1e"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (a low toxicity ratio solute : NF allows read-across to similar NFs)."	

Operators

function 'E-G-1e'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment															ELSE
C2	targ_NF	nil	ELSE														-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE													-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	gradual											ELSE	-
C5	medium_interaction.DN_dispersion_stability_in_medium_outcome	-	-	-	?	stable, intermediate									ELSE	-	-
C6	medium_interaction.DN_solutes_remain_their_form	-	-	-	-	?	Yes							No	-	-	-
C7	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	-	?	Yes						No	-	-	-
C8	targ_NF.density | density	-	-	-	-	-	-	?	density ≤ 1.0·g·cm⁻³			ELSE		-	-	-	-
C9	medium_interaction.DN_toxicity_ratio_ion_mol_vs_NF	-	-	-	-	-	-	-	?	low_ratio	ELSE		-	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	MI	MI	INCL	EXCL	EXCL	EXCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)									"Lethal and sub-lethal toxicity to representative aquatic species is dominated by the NF. Perform read-across to a similar NF. "	"Consider hypotheses E-G-1d+f on other toxicity ratios. "	"E-WS-2a-b on NFs in sediment."	"Characterise/ model the transformation process(es) and assess the “new” NFs."	"Character-ise/model the transformation process(es) and assess the “new” NFs."	"Consider hypotheses W-S-1a-b on unstable dispersions."	"Consider hypotheses E-G-1a-c."	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16

function 'E-G-1e'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_Dispersion_Info(tl).epqs	X
A3	result := result + DN_Density_Info(tl).epqs	X
A4	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-G-1f' is kind of 'E-G-1'

Hypothesis E-G-1f: NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (an intermediate toxicity ratio solute : NF limits possibilities for read-across).

Defined expressions

name	type	expression	comment
title	: String	"E-G-1f"	
lead	: String	"RIVM (Eric/Willie)"	
description	: String	"NFs that partially dissolve in a (partial) stable dispersion in environmentally relevant aquatic media: Following aqueous exposure lethal and sub-lethal toxicity to representative aquatic species is driven by the fate and toxicity characteristics of both NF particles and solutes in aqueous environments (an intermediate toxicity ratio solute : NF limits possibilities for read-across)."	

Operators

function 'E-G-1f'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment															ELSE
C2	targ_NF	nil	ELSE														–
C3	targ_medium as AquaticMedium | aquatic	–	nil	ELSE													–
C4	medium_interaction.DN_dissolution_in_medium_outcome	–	–	?	gradual											ELSE	–
C5	medium_interaction.DN_dispersion_stability_in_medium_outcome	–	–	–	?	stable, intermediate									ELSE	–	–
C6	medium_interaction.DN_solutes_remain_their_form	–	–	–	–	?	Yes							No	–	–	–
C7	medium_interaction.DN_NFs_remain_their_form	–	–	–	–	–	?	Yes						No	–	–	–
C8	targ_NF.density | density	–	–	–	–	–	–	?	density ≤ 1.0·g·cm⁻³			ELSE	–	–	–	–	–
C9	medium_interaction.DN_toxicity_ratio_ion_mol_vs_NF	–	–	–	–	–	–	–	?	intermediate_ratio	ELSE	–	–	–	–	–	–
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	MI	MI	MI	INCL	EXCL	EXCL	EXCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)									"Lethal and sub-lethal toxicity to representative aquatic species is a combination of both the NF and its solutes. Read-across is only possible when both dissolution and dispersion behaviour as well as toxicity behaviour is similar."	"Consider hypotheses E-G-1d-e on other toxicity ratios"	"E-WS-2a-b on NFs in sediment."	"Characterise/model the transformation process(es) and assess the “new” NFs."	"Characterise/model the transformation process(es) and assess the “new” NFs."	"Consider hypotheses W-S-1a-b on unstable dispersions."	"Consider hypotheses E-G-1a-c."	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16

function 'E-G-1f'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		–
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_Dispersion_Info(tl).epqs	X
A3	result := result + DN_Density_Info(tl).epqs	X
A4	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-G-2' is kind of 'E-G'

Hypothesis E-G-2: NFs with a very slow dissolution rate in environmentally relevant media: Biopersistence potential is likely which triggers (long-term) hazard concerns

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-G-2"	
lead	: String	"UNIVIE"	
description	: String	"NFs with a very slow dissolution rate in environmentally relevant media: Biopersistence potential is likely which triggers (long-term) hazard concerns"	
rationale	: String	"The hypothesis that materials can turn into structurally similar transformation products with similar mechanisms and degrees of toxicity is already acknowledged for the grouping of substances (ECHA, 2013) and will be an important justification for grouping in this hypothesis. Whilst the other environmental hypotheses deal only with the abiotic environmental fate of NFs, both E-G-2 and E-G-3 (very slow dissolving NFs have biopersistence potential) also have implications for the biological fate of NFs. NFs that are resistant to dissolution within biological fluids may be considered “”biopersistent."	

Operators

function 'E-G-2'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment					ELSE
C2	targ_NF	nil	ELSE				-
C3	targ_medium as AquaticMedium | aquatic	-	nil	ELSE			-
C4	targ_NF.DN_dissolution_outcome_in_fish_gut_saline	-	-	?	very_slow	ELSE	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	INCL	EXCL	IRR
A2	consequences→Add(#)				"Perform read-across for grouping to an analogue NF with similar surface chemistry and reactivity."	"Consider toxicity assessment on the basis of the molecule/ion formed, taking account of the place of release inside the organism."	
A3	group						
		R1	R2	R3	R4	R5	R6

function 'E-G-2'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_FishGutSaline_Info(tl).epqs	X
		R1

function 'E-G-2'::DN_Dissolution_FishGutSaline_Info(tl :: TierLevel) :: DN_Info

		TL1	ELSE
C1	tl		
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Screening dissolution test in static system according to OECD TG on Dissolution (Project 3.10, latest draft May 2018) in Fish gut saline."	
A3	result.preferred_methods		
A4	result.guidance_for_assay_selection		
A5	result.tier_escalation		
A6	/* Screening dissolution test in static system, Fish gut saline */	X	
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**, 'Gut saline medium')))	X	
		R1	R2

Class 'E-G-3' is kind of 'E-G'

Hypothesis E-G-5: Chemical speciation changes non-persistent NF to persistent NF
These hypotheses have been integrated into the other hypotheses

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-G-3"	
lead	: String	"UNIVIE/HWU/RIVM/UKRI"	
description	: String	"NF is chemically transformed into a “”new NF as a result of speciation with the surrounding medium: hazards are driven by the fate and hazard characteristics of the “”new NF."	

Operators

function 'E-G-3'::DN_DoSolutesFormNewNF_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Estimate element speciation with a model."	"Static flow test (ISO 19057:2017), in relevant medium follow by surface chemistry analysis "	"Continuous flow test (ISO 19057:2017), in relevant medium follow by surface chemistry analysis "	
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection				
A5	result.tier_escalation				
A6	/* Determine material solubility and element speciation with model, OECD TG 105 */	X			
A7					
A8	/* Screening solubility test in static system, OECD TG on Dissolution (Project 3.10, latest draft May 2018) */		X		
A9					
A10	/* Transmission electron microscopy (TEM) coupled with Energy Dispersive X-ray (EDX), ENV/JM/MONO(2016)7 */		X		
A11					
A12	/* Screening dissolution test in dynamic system */			X	
A13					
A14	/* Transmission electron microscopy (TEM) coupled with Energy Dispersive X-ray (EDX) */			X	
		R1	R2	R3	R4

function 'E-G-3'::DN_DoNFsTransformIntoNewNF_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Analysis of the surface chemistry in relevant environmental media."	
A3	result.preferred_methods		
A4	result.guidance_for_assay_selection		
A5	result.tier_escalation		
A6	/* Evolved-Gas Analysis (EGA), Adapted ISO/TS 11251:2019(en)? */		
A7	/* Thermogravimetric Analysis/Mass Spectrometry, ASTM E2105 - 00(2016) */		
A8	/* X-ray diffraction (XRD),ENV/JM/MONO(2016)7 */		
A9			
A10	/* Transmission electron microscopy (TEM) coupled with Energy Dispersive X-ray (EDX), ENV/JM/MONO(2016)7 */		
A11	result.epqs→Add(WTG(EPQ(PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC)))	X	
		R1	R2

function 'E-G-3'::DN_NewNFSurfaceProperties_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	ELSE
A1	result := DN_Info→**New**	X	X
A2	result.intro	"Analysis of the surface chemistry in relevant environmental media."	
A3	result.preferred_methods		
A4	result.guidance_for_assay_selection		
A5	result.tier_escalation		
A6	/* Evolved-Gas Analysis (EGA), ISO/TS 80004-6:2015 4.25 */	X	
A7	/* Thermogravimetric Analysis/Mass Spectrometry, Adapted ISO/TS 11251:2019(en)? */	X	
A8	/* Thermogravimetric Analysis/Infrared Analysis, ASTM E2105 - 00(2016) */	X	
A9	/* X-ray diffraction (XRD), ENV/JM/MONO(2016)7 */	X	
A10	/* Transmission electron microscopy (TEM) coupled with Energy Dispersive X-ray (EDX), ENV/JM/MONO(2016)7 */	X	
A11	/* ESR Spin trapping, ISO TS18827 (ISO2017) */	X	
		R1	R2

Class 'E-G-3a' is kind of 'E-G-3'

Hypothesis E-G-5a: "F for which dissolution products are chemically transformed into a "new" NF as a result of speciation with the surrounding medium: hazards are driven by the fate and hazard characteristics of the "new" biopersistent NF
These hypotheses have been integrated into the other hypotheses

Defined expressions

name	type	expression	comment
description	: String	"NF for which dissolution products are chemically transformed into a ""new NF as a result of speciation with the surrounding medium: hazards are driven by the fate and hazard characteristics of the ""new biopersistent NF"	

Operators

function 'E-G-3a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment				ELSE
C2	targ_NF	nil	ELSE			-
C3	medium_interaction.DN_solutes_remain_their_form	-	?	No	Yes	-
A1	**begin** outcome := #; result := outcome **end**	IRR	MI	INCL	EXCL	IRR
		R1	R2	R3	R4	R5

function 'E-G-3a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_DoSolutesFormNewNF_Info(tl).epqs	X
		R1

Class 'E-G-3b' is kind of 'E-G-3'

Hypothesis E-G-5: Chemical speciation changes non-persistent NF to persistent NF
These hypotheses have been integrated into the other hypotheses

Defined expressions

name	type	expression	comment
description	: String	"NF that are chemically transformed into a 'new' persistent NF as a result of speciation with the surrounding medium: hazards are driven by the hazard characteristics of the 'new' NF"	
rationale	: String	"The hypothesis that materials can turn into structurally similar transformation products with similar mechanisms and degrees of toxicity is already acknowledged for the grouping of substances (ECHA, 2013) and will be an important justification for grouping in this hypothesis. The main transformations of concern in the presented IATA are dissolution, redox/photo-reactions, sulphidation, phosphorylation and interaction of surrounding compounds with the NF. NFs that are resistant to dissolution within biological fluids may be considered more “”biopersistent."	

Operators

function 'E-G-3b'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment				ELSE
C2	targ_matr as Nanoform | new_NF	nil	ELSE			-
C3	medium_interaction.DN_NFs_remain_their_form	-	?	No	Yes	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	MI	INCL	EXCL	IRR

		R1	R2	R3	R4	R5

Class 'E-G-4' is kind of 'E-G'

Hypothesis E-G-4: Coating degradation (abiotic or biotic) influences dissolution, attachment efficiency and homo/heteroagglomeration.

Attributes

name	type	domain	inference	comment
'does coating persist'	:: YesNo			*Temp,*

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-G-4"	
lead	: String	"UK-CEH"	
description	: String	"Coating degradation (abiotic or biotic) influences NF dissolution, attachment efficiency, homo/heteroagglomeration, and toxicity."	
rationale	: String	"WP4 elements of this hypothesis identify surface treatments that may be classed as “readily ”biodegradable. Grouping in hypotheses E-G-4a-c provide justification of waiving surface treatment as a property in similarity assessment. This is on the basis that the poor durability of the surface treatment means that the “coated ”form is unlikely to be the form present in exposures. This forms part of the read-across justification between surface treated target NFs and a non-coated source analogue, or between candidate NFs with different surface treatments. Definition of Readily biodegradable according to the OECD (OECD Test Guideline 301: Ready biodegradability: https://doi.org/10.1787/9789264070349-en)“ An arbitrary classification of chemicals which have passed certain specified screening tests for ultimate biodegradability; these tests are so stringent that it is assumed that such compounds will rapidly and completely biodegrade in aquatic environments under aerobic ”conditions. This hypothesis has been split into three sub-hypotheses (a-c) respectively in WWTP, aquatic and soil compartments. Sediments are not included in this hypothesis to date due to (co-)occurrence of anaerobic conditions and uncertainty over the applicability of this rationale for biodegradation that specifies degradation under aerobic conditions (see definition above). Key is that if surface treated NFs are grouped in E-G-4 a-c, then the surface treatment is not considered relevant in the exposure and so may be waived as a property when considering similarity between NFs. If NF not grouped in E-G-4a-c, surface treatment must always be considered in a similarity assessment by default. If a surface treated NF is not lost and thus E-G-4 a-c rejected, surface treated NFs may still be grouped in other hypotheses (e.g. in one of the E-G-1 hypotheses). However, in these cases it must be demonstrated that the surface treatments are similar between the NFs (through rules either like the ECETOC rules, or though assessment of structural similarity such as the AMBIT tool)."	

Operators

function 'E-G-4'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	targ_matr as Nanoform | nm	nil	ELSE	
C2	targ_medium as AquaticMedium | auq	-	nil	ELSE
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR
		R1	R2	R3

function 'E-G-4'::DN_BiodegradableOrganicCoatingInWWTP_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3
A1	result := DN_Info→**New**	X	X	X
A2	result.intro	"Biodegradation screening MT2 in activated sludge."	"Regulatory accepted screening tests for biodegradation in WWTP."	"Regulatory accepted simulation tests for biodegradation in WWTP or wastewater discharges."
A3	result.preferred_methods			
A4	result.guidance_for_assay_selection			
A5	result.tier_escalation			
A6	/* Biodegradation- MT2 screen, GRACIOUS MT2 SOP under development */	X		
A7	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MT-2 screening Assay'), 2.0·d)))	X		
A8	/* Biodegradation- DOC Die-Away, OECD 301a */		X	
A9	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation DOC Die-Away Assay'), 10.0·d)))		X	
A10	/* Biodegradation- CO2 Evolution, OECD 301b */		X	
A11	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation CO2 Evolution Assay'), 10.0·d)))		X	
A12	/* Biodegradation- MITI (I), OECD 301c */		X	
A13	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MITI (I) Assay'), 10.0·d)))		X	
A14	/* Biodegradation- Closed Bottle, OECD 301e */		X	
A15	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Closed Bottle Assay'), 10.0·d)))		X	
A16	/* Biodegradation- Modified OECD Screening, OECD 301d */		X	
A17	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Modified OECD screening Assay'), 10.0·d)))		X	
A18	/* Biodegradation- Manometric Respirometry, OECD 301f, ISO 14851 2019 */		X	
A19	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Manometric Respirometry Assay'), 10.0·d)))		X	
A20	/* Biodegradation- Aerobic sewage, OECD 303 */			X
A21	result.epqs→Add(WTG(DUR(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation Aerobic sewage Assay'), 21.0·d)))			X
A22	/* Biodegradation- wastewater discharge, OECD 314 A t/m E */			X
A23	result.epqs→Add(WTG(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation wastewater discharge, sewer systems Assay')))			X
A24	result.epqs→Add(WTG(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation wastewater discharge, activated sludge Assay')))			X
A25	result.epqs→Add(WTG(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation wastewater discharge, anaerobic digester sludge')))			X
A26	result.epqs→Add(WTG(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation wastewater discharge, treated effluent **in** the mixing zone **of** surface water')))			X
A27	result.epqs→Add(WTG(ASSAY(EPQ(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG), 'Biodegradation wastewater discharge, untreated wastewater that **is** directly discharged **to** surface water')))			X
		R1	R2	R3

function 'E-G-4'::DN_BiodegradableOrganicCoatingInAquaticComp_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	ELSE
A1	result := DN_Info→**New**	X	X	X
A2	result.intro	"Biodegradation screening MT2 in surface water. Direct photolysis theoretical screening."	"Regulatory accepted screening tests for biodegradation in surface waters and/or direct photolysis in surface waters."	
A3	result.preferred_methods			
A4	result.guidance_for_assay_selection			
A5	result.tier_escalation			
A6	/* Biodegradation- MT2 screen, GRACIOUS MT2 SOP under development */	X		
A7	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MT-2 screening Assay'), 2.0·d)))	X		
A8	/* Direct photolysis theoretical screen, OECD 316 */	X		
A9				
A10	/* Biodegradation- DOC Die-Away, OECD 301a */		X	
A11	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation DOC Die-Away Assay'), 10.0·d)))		X	
A12	/* Biodegradation- CO2 Evolution, OECD 301b */		X	
A13	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation CO2 Evolution Assay'), 10.0·d)))		X	
A14	/* Biodegradation- MITI (I), OECD 301c */		X	
A15	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MITI (I) Assay'), 10.0·d)))		X	
A16	/* Biodegradation- Closed Bottle, OECD 301e */		X	
A17	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Closed Bottle Assay'), 10.0·d)))		X	
A18	/* Biodegradation- Modified OECD Screening, OECD 301d */		X	
A19	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Modified OECD screening Assay'), 10.0·d)))		X	
A20	/* Biodegradation- Manometric Respirometry, OECD 301f, ISO 14851 2019 */		X	
A21	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Manometric Respirometry Assay'), 10.0·d)))		X	
		R1	R2	R3

function 'E-G-4'::DN_BiodegradableOrganicCoatingInSoilComp_Info(tl :: TierLevel):: DN_Info

C1	tl	TL1	TL2	TL3
A1	result := DN_Info→**New**	X	X	X
A2	result.intro	"Biodegradation screening MT2 with soil community. Direct photolysis theoretical screening."	"Regulatory accepted screening tests for biodegradation in surface waters and/or direct photolysis in surface waters."	
A3	result.preferred_methods			
A4	result.guidance_for_assay_selection			
A5	result.tier_escalation			
A6	/* Biodegradation- MT2 screen, GRACIOUS MT2 SOP under development */	X		
A7	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MT-2 screening Assay'), 2.0·d)))	X		
A8	/* Direct photolysis theoretical screen, OECD 316 */	X		
A9				
A10	/* Biodegradation- DOC Die-Away, OECD 301a */		X	
A11	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation DOC Die-Away Assay'), 10.0·d)))		X	
A12	/* Biodegradation- CO2 Evolution, OECD 301b */		X	
A13	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation CO2 Evolution Assay'), 10.0·d)))		X	
A14	/* Biodegradation- MITI (I), OECD 301c */		X	
A15	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation MITI (I) Assay'), 10.0·d)))		X	
A16	/* Biodegradation- Closed Bottle, OECD 301e */		X	
A17	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Closed Bottle Assay'), 10.0·d)))		X	
A18	/* Biodegradation- Modified OECD Screening, OECD 301d */		X	
A19	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Modified OECD screening Assay'), 10.0·d)))		X	
A20	/* Biodegradation- Manometric Respirometry, OECD 301f, ISO 14851 2019 */		X	
A21	result.epqs→Add(WTG(DUR(EPQMA(EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG, 'OECD TG301 mineral medium', 'Biodegradation Manometric Respirometry Assay'), 10.0·d)))		X	
A22	/* Photodegradation at soil surface ??? */			
		R1	R2	R3

Class 'E-G-4b' is kind of 'E-G-4'

Hypothesis E-G-4b: NFs with a chemical coating that is lost from the NF surface following exposure in aquatic compartment can be grouped: : Fate and toxicity of the exposure relevant NF can be considered similar to a non-coated analogous NF in aquatic compartment.

Defined expressions

name	type	expression	comment
title	: String	"E-G-4b"	
description	: String	"NFs with a chemical coating that is lost from the NF surface following exposure in aquatic compartment can be grouped: : Fate and toxicity of the exposure relevant NF can be considered similar to a non-coated analogous NF in aquatic compartment."	

Operators

function 'E-G-4b'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment										ELSE
C2	targ_matr as Nanoform | nm	nil	ELSE									-
C3	targ_medium as AquaticMedium | aqua	-	nil	ELSE								-
C4	env_compartment as Water	-	-	nil	ELSE							-
C5	Hyp('E-G-1b').outcome	-	-	-	INCL						ELSE	-
C6	nm.organic_coatings | coatings	-	-	-	0	ELSE					-	-
C7	medium_interaction.DN_biodegradable_organic_coatings_present	-	-	-	-	?	Yes		No	ELSE	-	-
C8	medium_interaction.DN_biodegradable_organic_coatings	-	-	-	-	-	0	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	EXCL	MI	MI	INCL	EXCL	MI	IRR	IRR
A2	consequences→Add(#)				"NF is a non organic coated material."			"Read-across to non-coated analogous NF as the new target NF for grouping by “where they go"	"Consider organic surface treatment to be durable and environmental exposure to be to the core and surface treatment combined. Consider alternative environmental hypotheses for the surface treated NF."			
A3	'missing info'						"No biodegradable organic coating assigned yet!"					
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11

function 'E-G-4b'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_BiodegradableOrganicCoatingInAquaticComp_Info(tl).epqs	X
		R1

Class 'E-G-4c' is kind of 'E-G-4'

Hypothesis E-G-4c: NFs with a chemical coating that is lost from the NF surface following exposure in soil compartment can be grouped: Exposure relevant NF can be considered similar to a non-coated analogous NF in soil compartment

Defined expressions

name	type	expression	comment
title	: String	"E-G-4c"	
description	: String	"NFs with a chemical coating that is lost from the NF surface following exposure in soil compartment can be grouped: Exposure relevant NF can be considered similar to a non-coated analogous NF in soil compartment."	

Operators

function 'E-G-4c'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment									ELSE
C2	targ_matr as Nanoform | nm	nil	ELSE								-
C3	targ_medium as SoilMedium | soil	-	nil	ELSE							-
C4	env_compartment as Soil | soil_comp	-	-	nil	ELSE						-
C5	nm.organic_coatings | coatings	-	-	-	0	ELSE					-
C6	medium_interaction.DN_biodegradable_organic_coatings_present	-	-	-	-	?	Yes		No	ELSE	-
C7	medium_interaction.DN_biodegradable_organic_coatings	-	-	-	-	-	0	ELSE	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	IRR	EXCL	MI	MI	INCL	EXCL	MI	IRR

A2	consequences→Add(#)				"NF is a non-organic coated material."			"Read-across to non- organic coated analogous NF as the new target NF for grouping by “where they go”."	"Consider organic coating to be durable and environmental exposure to be to the core and coating combined."		
A3	'missing info'						"No biodegradable organic coating assigned yet!"				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

function 'E-G-4c'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_BiodegradableOrganicCoatingInSoilComp_Info(tl).epqs	X
		R1

Class 'E-G-4a' is kind of 'E-G-4'

Hypothesis E-G-4a: NFs with a chemical coating that is lost from the NF surface following exposure in WWTP compartment can be grouped: Fate and toxicity of the exposure relevant NF can be considered similar to a non-coated analogous NF in WWTP compartment.

Defined expressions

name	type	expression	comment
title	: String	"E-G-4a"	
description	: String	"NFs with a chemical coating that is lost from the NF surface following exposure in WWTP compartment can be grouped: Fate and toxicity of the exposure relevant NF can be considered similar to a non-coated analogous NF in WWTP compartment."	

Operators

function 'E-G-4a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment									ELSE
C2	targ_NF	nil	ELSE								-
C3	targ_medium as AquaticMedium | aqua	-	nil	ELSE							-
C4	env_compartment as WWTP | wwtp	-	-	nil	ELSE						-
C5	targ_NF.organic_coatings | coatings	-	-	-	0	ELSE					-
C6	medium_interaction.DN_biodegradable_organic_coatings_present	-	-	-	-	?	Yes		No	ELSE	-
C7	medium_interaction.DN_biodegradable_organic_coatings	-	-	-	-	-	0	ELSE	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	EXCL	MI	MI	INCL	EXCL	MI	IRR
A2	consequences→Add(#)				"NF is a non- organic coated material"			"Aquatic exposure on release from WWTP may be considered to be of the non-organic coated particle "	"Consider coating to be durable and environmental exposure to be to the core and coating combined."		
A3	'missing info'						"No biodegradable organic coating assigned yet!"				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

function 'E-G-4a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_BiodegradableOrganicCoatingInWWTP_Info(tl).epqs	X
		R1

Class 'E-G-4d' is kind of 'E-G-4'

Hypothesis E-G-4d: NFs with a durable and toxic organic surface treatment cannot be grouped for read-across in any environmental/system compartment : Specific testing is required.

Defined expressions

name	type	expression	comment
title	: String	"E-G-4d"	
description	: String	"NFs with a durable and toxic organic surface treatment cannot be grouped for read-across in any environmental/system compartment : Specific testing is required."	

Operators

function 'E-G-4d'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment								ELSE
C2	targ_NF	nil	ELSE							-
C3	targ_NF.organic_coatings	-	0	ELSE						-
C4	medium_interaction.DN_biodegradable_organic_coatings_present	-	-	?	Yes	No				-
C5	medium_interaction.non_biodegradable_organic_coatings | persistent_coatings	-	-	-	-	0	ELSE			-
C6	persistent_coatings→ForAll(c | Known(c.hazardous_to_aquatic_environment))	-	-	-	-	-	True		False	-
C7	persistent_coatings→Exists(c | c.hazardous_to_aquatic_environment = Yes)	-	-	-	-	-	True	False	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	EXCL	MI	EXCL	EXCL	INCL	EXCL	MI	IRR

A2	consequences→Add(#)		"NF is a non-organic coated material."		"Organic surface treatment is poorly durable. 'Non-coated' analogous NF considered the new target NF"	"Should not happen!"	"Specific hazard assessment required as surface treatment contributes to toxicity of the NF suspension. NF may not be grouped."	"Surface treated NF remains target NF. Influence of this surface treatment on fate of the NF must be considered in relevant environmental hypotheses."		
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'E-G-4d'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	/* Depends on compartment WWTP, Aquatic or Soil, covered by E-G-4a,b,c */	
		R1

Class 'E-WS' is kind of EnvHypothesis

Hypothesis E-WS: Water Sediment related IATAs

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-WS-1"	
lead	: String	"HWU/RIVM (Simon/Willie)"	
description	: String	"Specific NF properties will define their stability in aquatic systems; poorly stable NFs will tend to settle leading to high exposure in benthic systems."	

Operators

function 'E-WS'::DN_Dissolution_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	ELSE
A1	result := DN_Info→**New**	X	X	X
A2	result.intro	"Batch dissolution test (24h, 3 pH levels, 5 mM sodium bicarbonate buffer)"	"Continuous flow test (24h, 3 pH levels, OECD TG 318 medium with NOM)"	
A3	result.preferred_methods			
A4	result.guidance_for_assay_selection			
A5	result.tier_escalation			
A6	/* Batch dissolution test, ISO 19057:2017 */	X		
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 5')))	X		
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 7')))	X		
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 9')))	X		
A10	/* Continuous flow system, ISO 19057:2017 */		X	
A11	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 4')))		X	
A12	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 7')))		X	
A13	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 9')))		X	
		R1	R2	R3

function 'E-WS'::DN_ToxicityRatio_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Acute toxicity testing w/ benthic species."	"Chronic toxicity testing single species OECD TG."	"Chronic toxicity testing single species OECD TG w/ aged NFs. Microcosm/mesocosm studies."	
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection				
A5	result.tier_escalation				
A6	/* Microtox assay (Vibrio fischeri), Environment Canada (2002) EPS 1/RM/42 */	X			
A7					
A8	/* Caenorhabditis elegans sediment toxicity test, ISO 10872:2010 */	X			
A9	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%), 'Caenorhabditis elegans sediment toxicity test'), 'M9 medium')))	X			
A10	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·l^{-1}), EC_x), 50.0·%), 'Caenorhabditis elegans sediment toxicity test'), 'M9 medium')))	X			
A11	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%), 'Caenorhabditis elegans sediment toxicity test'), 'ISO artificial sediment + M9 medium')))	X			
A12	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·l^{-1}), EC_x), 50.0·%), 'Caenorhabditis elegans sediment toxicity test'), 'ISO artificial sediment + M9 medium')))	X			
A13	/* Water-sediment Myriophyllum spicantum toxicity test, OECD 239 */		X		
A14	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%), 'Water-sediment Myriophyllum spicantum toxicity test'), 'OECD 219 sediment + Smart **and** Barko medium')))		X		
A15	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·l^{-1}), EC_x), 50.0·%), 'Water-sediment Myriophyllum spicantum toxicity test'), 'OECD 219 sediment + Smart **and** Barko medium')))		X		
A16	/* Sediment-water Lumbriculus toxicity test using spiked sediment, OECD 225 */		X		
A17	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_SURVIVAL, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Lumbriculus toxicity test using spiked sediment'), 'OECD 203 water + OECD 225 sediment')))		X		
A18	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Lumbriculus toxicity test using spiked sediment'), 'OECD 203 water + OECD 225 sediment')))		X		
A19	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Lumbriculus toxicity test using spiked sediment'), 'OECD 203 water + OECD 225 sediment')))		X		
A20	/* Sediment-water Chironomid spiked sediment toxicity test, OECD 218 */		X		
A21	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_EMERGENCE, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 218 conforming water + sediment')))		X		
A22	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_DEVELOPMENT, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 218 conforming water + sediment')))		X		
A23	/* Sediment-water Chironomid spiked sediment toxicity test, OECD 219 */		X		
A24	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_EMERGENCE, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 218 conforming water + sediment')))		X		
A25	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_DEVELOPMENT, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 218 conforming water + sediment')))		X		
A26	/* Sediment-water Chironomid spiked sediment toxicity test, OECD 233 */		X		
A27	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_EMERGENCE, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A28	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_DEVELOPMENT_RATE, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A29	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_SEX_RATIO, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A30	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·kg^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A31	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_EMERGENCE, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A32	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_DEVELOPMENT_RATE, ·mg·l^{-1}), EC_x), 50.0·%), 'Sediment-water Chironomid spiked sediment toxicity test'), 'OECD 233 conforming water + sediment')))		X		
A33	/* Leptocherius plumulosus chronic marine and estuarine sediment toxicity test, EPA 600/R-01/020 */		X		
A34	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_SURVIVAL, ·mg·kg^{-1}), LC_x), 50.0·%), 'Leptocherius plumulosus chronic marine **and** estuarine sediment toxicity test'), 'Natural marine/estuarine sediment + water')))		X		
A35	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·kg^{-1}), LC_x), 50.0·%), 'Leptocherius plumulosus chronic marine **and** estuarine sediment toxicity test'), 'Natural marine/estuarine sediment + water')))		X		
A36	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·kg^{-1}), LC_x), 50.0·%), 'Leptocherius plumulosus chronic marine **and** estuarine sediment toxicity test'), 'Natural marine/estuarine sediment + water')))				
A37	/* Water-sediment Myriophyllum spicantum toxicity test, OECD 239 AGED NF! */			X	
A38					
A39	/* Sediment-water Lumbriculus toxicity test using spiked sediment, OECD 225 AGED NF! */			X	
A40					
A41	/* Leptocherius plumulosus chronic marine and estuarine sediment toxicity test, EPA 600/R-01/020 AGED NF */			X	
A42					
A43	/* Simulated freshwater lentic field tests (outdoor microcosm and mesocosms), OECD TG 53 */				
A44	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_SURVIVAL, ·mg·kg^{-1}), LC_x), 50.0·%), 'Simulated freshwater lentic field test'), 'Natural freshwater + sediment')))			X	
A45	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_GROWTH, ·mg·kg^{-1}), LC_x), 50.0·%), 'Simulated freshwater lentic field test'), 'Natural freshwater + sediment')))			X	
A46	result.epqs→Add(WTD(MED(ASSAY(PER(ENUM(EPQU(EC_SEDIMENT_TOX::EP_REPRODUCTION, ·mg·kg^{-1}), LC_x), 50.0·%), 'Simulated freshwater lentic field test'), 'Natural freshwater + sediment')))			X	
		R1	R2	R3	R4

Class 'E-WS-1' is kind of 'E-WS'

Hypothesis E-WS-1

Defined expressions

name	type	expression	comment
rationale	: String	"Heteroaggregation with suspended particulate matter (SPM) is the dominant force by which NFs are removed from the aquatic compartment. Heteroaggregation is measured via attachment efficiency α(- propensity for NFs and SPM to successfully ‘’attach to one another upon colliding). Sensitivity analysis predicts NF fate in aquatic compartment will be dominated by heteroaggregation when α≥ 1.1 x 10-4 (Meesters et al., 2019). This aquatic fate is no longer in E-WS-1 as has been incorporated in E-G-1. If sediment exposure is anticipated, bioavailable NF concentrations ‘(’free material plus material <0.45 µm) become sensitive to dissolution if the rate is > 1.1 x 10-8 s-1 (Meesters et al., 2019). Below this value, NFs are insensitive and will persist in bioavailable sediment fractions. Lethal and sub-lethal toxicity outcomes to representative benthic species are dependent on dissolution in sediment and the contribution of the NF and dissolution products. "	

Class 'E-WS-1a' is kind of 'E-WS-1'

Hypothesis E-WS-1a: Bioavailable NFs with a very slow dissolution rate in sediment can be grouped: Following sediment exposure, NFs in this group will maintain nano-specific activity and can cause lethal and sub-lethal toxicity to representative benthic species.

Defined expressions

name	type	expression	comment
title	: String	"E-WS-2a"	
description	: String	"Bioavailable NFs with a very slow dissolution rate in sediment can be grouped: Following sediment exposure, NFs in this group will maintain nano-specific activity and can cause lethal and sub-lethal toxicity to representative benthic species."	

Operators

function 'E-WS-1a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment							ELSE
C2	targ_NF | nf	nil	ELSE						-
C3	env_compartment is Sediment	-	True					False	-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	?	very_slow			ELSE	-	-
C5	medium_interaction.DN_NFs_remain_their_form	-	-	?	Yes	No	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	MI	MI	INCL	EXCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"Bioavailable NF will maintain nano-specific activity in sediment. Consider chronic NF toxicity in sediment. "	"Characterise/model the transformation process(es) and assess the 'new' NFs"	"Bioavailable NF concentration in sediment is sensitive to dissolution. Consider E-WS-1b-e."		
		R1	R2	R3	R4	R5	R6	R7	R8

function 'E-WS-1a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
		R1

Class 'E-WS-1b' is kind of 'E-WS-1'

Hypothesis E-WS-1b: Bioavailable NFs with a quick dissolution rate in sediment can be grouped: Following sediment exposure, the dissolution products of NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species.

Defined expressions

name	type	expression	comment
title	: String	"E-WS-2b"	*Bioavailable NFs with a quick dissolution rate in sediment can be grouped: Following sediment exposure, the dissolution products of NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species.*
description	: String	"Bioavailable NFs with a quick dissolution rate in sediment can be grouped: Following sediment exposure, the dissolution products of NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species."	

Operators

function 'E-WS-1b'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment								ELSE
C2	targ_NF | nf	nil	ELSE							-
C3	env_compartment is Sediment	-	True						False	-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	?	very_slow		quick		gradual	-	-
C5	medium_interaction.DN_solutes_remain_their_form	-	-	-	?	Yes	No	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	MI	EXCL	MI	INCL	EXCL	EXCL	IRR	IRR

A2	consequences→Add(#)			"Bioavailable NFs will maintain nanospecific activity in sediment. Consider E-WS-1a."		"Lethal and sub-lethal toxicity to representative benthic species is caused by dissolution products. Perform read-across to dissolution products."	"Characterise/model the transformation process(es) and assess the “new” NFs."	"Bioavailable NF is partially dissolving in sediment. Consider E-WS-1c-e."		
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'E-WS-1b'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
		R1

Class 'E-WS-1c' is kind of 'E-WS-1'

Hypothesis E-WS-1c: Bioavailable NFs that partially dissolve in sediment and have a low toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species.

Defined expressions

name	type	expression	comment
title	: String	"E-WS-2c"	
description	: String	"Bioavailable NFs that partially dissolve in sediment and have a low toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species."	

Operators

function 'E-WS-1c'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment														ELSE
C2	targ_NF	nil	ELSE													–
C3	env_compartment is Sediment	–	False	True												–
C4	targ_medium as SedimentMedium | sediment	–	–	nil	ELSE											–
C5	medium_interaction.DN_dissolution_in_medium_outcome	–	–	–	?	very_slow	quick	gradual								–
C6	medium_interaction.DN_solutes_remain_their_form	–	–	–	–	–	–	?	Yes						No	–
C7	medium_interaction.DN_NFs_remain_their_form	–	–	–	–	–	–	–	?	Yes				No	–	–
C8	sediment.toxicity_ratio_ion_mol_vs_NF	–	–	–	–	–	–	–	–	?	low_ratio	ELSE		–	–	–
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	IRR	MI	EXCL	EXCL	MI	MI	MI	INCL	EXCL		EXCL	EXCL	IRR
A2	consequences→Add(#)					"Bioavailable NFs will maintain nano-specific activity in sediment. Consider E-WS-2a"	"Consider E-WS-2b"				"Lethal and sub-lethal toxicity to representat-ive benthic species is dominated by the NF. Read-across to ana-logous source material jus-tified."	"Lethal and sub-lethal toxicity to representat-ive benthic species is not domin-ated by the NF. Consider E-WS-1d-e."		"Character-ise/model the transformation process(es) and assess the “new” NFs."	"Character-ise/model the transformation process(es) and assess the “new” NFs."	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11		R12	R13	R14

function 'E-WS-1c'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		–
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-WS-1d' is kind of 'E-WS-1'

Hypothesis E-WS-1d: Bioavailable NFs that partially dissolve in sediment and have a high toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, the dissolution products of NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species.

Defined expressions

name	type	expression	comment
title	: String	"E-WS-2d"	
description	: String	"Bioavailable NFs that partially dissolve in sediment and have a high toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, the dissolution products of NFs in this group can cause lethal and sub-lethal toxicity to representative benthic species."	

Operators

function 'E-WS-1d'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment												ELSE
C2	targ_NF	nil	ELSE											-
C3	env_compartment is Sediment	-	True										False	-
C4	targ_medium as SedimentMedium | sediment	-	nil	ELSE									-	-
C5	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow	quick	gradual						-	-
C6	medium_interaction.DN_solutes_remain_their_form	-	-	-	-	-	?	Yes				No	-	-
C7	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	-	-	?	Yes			No	-	-
C8	sediment.toxicity_ratio_ion_mol_vs_NF	-	-	-	-	-	-	-	?	high_ratio	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	EXCL	EXCL	MI	MI	MI	INCL	EXCL	EXCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"Bioavail-able NFs will maintain nano-specific activity in sediment. Con-sider E-WS-1a"	"Consider E-WS-1b"				"Lethal and sub-lethal toxicity to representative benthic species is dominated by the solute(s). Per-form read-across for solute(s). "	"Lethal and sub-lethal toxicity to representative benthic species is not dominated by the constituent ions/ molecules. Consider E-WS-1c or e. "				
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14

function 'E-WS-1d'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-WS-1e' is kind of 'E-WS-1'

Hypothesis E-WS-1e: Bioavailable NFs that partially dissolve in sediment and have an intermediate toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, NFs in this group, together with their dissolution products can cause lethal and sub-lethal toxicity to representative benthic species.

Defined expressions

name	type	expression	comment
title	: String	"E-WS-e2"	
description	: String	"Bioavailable NFs that partially dissolve in sediment and have an intermediate toxicity ratio dissolution products:NF can be grouped: Following sediment exposure, NFs in this group, together with their dissolution products can cause lethal and sub-lethal toxicity to representative benthic species."	

Operators

function 'E-WS-1e'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment													ELSE
C2	targ_NF	nil	ELSE												-
C3	env_compartment is Sediment	-	True											False	-
C4	targ_medium as SedimentMedium | sediment	-	nil	ELSE										-	-
C5	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow	quick	gradual							-	-
C6	medium_interaction.DN_solutes_remain_their_form	-	-	-	-	-	?	Yes					No	-	-
C7	medium_interaction.DN_NFs_remain_their_form	-	-	-	-	-	-	?	Yes			No	-	-	-
C8	sediment.toxicity_ratio_ion_mol_vs_NF	-	-	-	-	-	-	-	?	intermediate_ratio	ELSE	-	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	EXCL	EXCL	MI	MI		INCL	EXCL	EXCL	EXCL	IRR	IRR
A2	consequences→Add(#)				"Bioavailable NFs will maintain nano-specific activity in sediment. Consider E-WS-1a"	"Consider E-WS-1b"				"NF and dissolution products both contribute to lethal and sub-lethal toxicity in representative benthic species. Specific testing may be required."	"Lethal and sub-lethal toxicity to representative benthic species is dominated by either the NF or dissolution products. Consider E-WS-1c or d."	"Characterise/model the transformation process(es) and assess the “new” NFs."	"Characterise/model the transformation process(es) and assess the “new” NFs."		
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14

function 'E-WS-1e'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_ToxicityRatio_Info(tl).epqs	X
		R1

Class 'E-S' is kind of EnvHypothesis

Hypothesis E-S: Soil related IATAs

Defined expressions

name	type	expression	comment
rationale	: String	"IATA provide a tiered testing strategy to group NF in soils according to dissolution and attachment. This is distinct from E-G-2, which applies within the aquatic compartment as rather than indicating stability and thus transport to sediment (E-G-2), it assesses transport within the soil to direct what hazard testing is appropriate Currently, E-S…- are focused on delivering the most relevant toxicity assays to correctly assess the risk of the NF based on knowledge of “where they ”go in the soils. E-S-1 identifies NF which do not dissolve in the soils within the residence time and so chronic testing is recommended E-S-2 identifies NF for which dissolution rates drive fate and potentially hazard, and where aging of NFs is recommended prior to testing. Category approaches to read-across (identification of a regular pattern) may be applicable for partially dissolving NFs"	

Operators

```
function 'E-S'::DN_Dissolution_Info( tl :: TierLevel ):: DN_Info
```

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→New	X	X	X	X
A2	result.intro	"Batch dissolution test (24h, 3 pH levels, 5 mM sodium bicarbonate buffer)."	"Continuous flow test (24h, 3 pH levels, OECD TG 318 medium with NOM)."	"Continuous flow test (24hin simulated soil pore water conditions)."	
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection				
A5	result.tier_escalation				
A6	/* Batch dissolution test, ISO 19057:2017 */	X			
A7	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 5')))	X			
A8	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 7')))	X			
A9	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, '5 mM sodium bicarbonate buffer, pH 9')))	X			
A10	/* Continuous flow system,ISO 19057:2017 */				
A11	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 4')))		X		
A12	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 7')))		X		
A13	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'OECD TG318 medium + NOM, pH 9')))		X		
A14	/* Continuous flow system,ISO 19057:2017 in relevant soil medium */				
A15	result.epqs→Add(WTG(EPQM(PC_WATER_SOL::EP_DISSOLUTION_RATE, 'Relevant soil medium')))			X	
		R1	R2	R3	R4

function 'E-S'::DN_SolidPhaseAffinity_Info(tl :: TierLevel) :: DN_Info

C1	tl	TL1	TL2	TL3	ELSE
A1	result := DN_Info→**New**	X	X	X	X
A2	result.intro	"Screening dispersion test, Screening batch retention test."	"Extended dis- persion test- SPM (OECD 318)."	"Column leaching test (OECD 312)."	
A3	result.preferred_methods				
A4	result.guidance_for_assay_selection				
A5	result.tier_escalation				
A6	/* Screening dispersion test- SPM, OECD 318 */	X			
A7	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)')))	X			
A8	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)')))	X			
A9	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)')))	X			
A10	/* Screening batch retention test, NanoFASE1 (based on OECD 106) */	X			
A11	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_BATCH_RETENTION_COEFFICIENT, '0.01 mM CaCl2')))	X			
A12	/* Extended dispersion test- SPM, OECD 318 */		X		
A13	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)')))		X		
A14	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)')))		X		
A15	result.epqs→Add(WTG(EPQM(EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY, 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)')))		X		
A16	/* Column leaching test, OECD 312*/			X	
A17					
		R1	R2	R3	R4

Class 'E-S-1' is kind of 'E-S'

Hypothesis E-S-1

Defined expressions

name	type	expression	comment
lead	: String	"UKRI"	

Operators

function 'E-S-1'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
		R1

Class 'E-S-1a' is kind of 'E-S-1'

Hypothesis E-S-1a: NFs with a very slow dissolution rate and low affinity with the solid soil phase: Following soil exposure NF mobility in soil follows ground water flows. Acute toxicity of NFs to terrestrial organisms should be considered.

Defined expressions

name	type	expression	comment
title	: String	"E-S-1a"	
description	: String	"NFs with a very slow dissolution rate and low affinity with the solid soil phase: Following soil exposure NF mobility in soil follows ground water flows. Acute toxicity of NFs to terrestrial organisms should be considered."	

Operators

function 'E-S-1a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment									ELSE
C2	targ_NF	nil	ELSE								-
C3	env_compartment as Soil | soil	-	nil	ELSE							-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow					ELSE	-
C5	medium_interaction.DN_NFs_remain_their_form	-	-	-	?	Yes			No	-	-
C6	medium_interaction.DN_affinity_to_solid_soil_phase	-	-	-	-	?	low_affinity	ELSE	-	-	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	MI	MI	INCL	EXCL	EXCL	EXCL	IRR
A2	consequences→Add(#)						"Target NF is recommended for testing. Read-across to analogous source material for acute soil toxicity studies is justified."	"Fate of NF in soils becomes sensitive to stability of the NF against aggregation. NF may be considered mobile in soil pore water and will be lost periodically under saturated conditions (E-S-1b)."	"Transformed NF must be tested against all hypotheses"	"Fate of NF in soils becomes sensitive to dissolution. (E-S-2)"	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

function 'E-S-1a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_SolidPhaseAffinity_Info(tl).epqs	X
		R1

Class 'E-S-1b' is kind of 'E-S-1'

Hypothesis E-S-1b: NFs with a very slow dissolution rate and high affinity with the solid soil phase: Following soil exposure persistence in soil is likely which triggers (long-term) toxicity concerns.

Defined expressions

name	type	expression	comment
title	: String	"E-S-1b"	
description	: String	"NFs with a very slow dissolution rate and high affinity with the solid soil phase: Following soil exposure persistence in soil is likely which triggers (long-term) toxicity concerns."	

Operators

function 'E-S-1b'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment									ELSE
C2	targ_NF	nil	ELSE								-
C3	env_compartment as Soil | soil	-	nil	ELSE							-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	very_slow					ELSE	-
C5	medium_interaction.DN_NFs_remain_their_form	-	-	-	?	Yes			No	-	-
C6	medium_interaction.DN_affinity_to_solid_soil_phase	-	-	-	-	?	high_affinity	ELSE	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	MI	MI	MI	INCL	EXCL	EXCL	EXCL	IRR

A2	consequences→Add(#)						"Chronic or long-term testing recommended."		"Transformed NF must be tested against all hypotheses"	"Fate of NF in soils becomes sensitive to dissolution. (E-S-2)"	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

function 'E-S-1b'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2	result := result + DN_SolidPhaseAffinity_Info(tl).epqs	X
		R1

Class 'E-S-2' is kind of 'E-S'

Hypothesis E-S-2: NF with a very slow dissolution rate and low affinity with the solid soil phase: Mobility potential is likely under saturated conditions which triggers acute hazard concerns

Class 'E-S-2a' is kind of 'E-S-2'

Hypothesis E-S-2a: NFs with a quick dissolution rate in soil: Following soil exposure fate is driven by dissolution rather than mobility of the NFs.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-S-2a"	
description	: String	"NFs with a quick dissolution rate in soil: Following soil exposure fate is driven by dissolution rather than mobility of the NFs."	

Operators

function 'E-S-2a'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment								ELSE
C2	targ_NF	nil	ELSE							-
C3	env_compartment as Soil | soil	-	nil	ELSE						-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	instantaneously, quick			gradual	very_slow	-
C5	medium_interaction.DN_solutes_remain_their_form	-	-	-	?	Yes	No	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		IRR	IRR	MI	MI	INCL	EXCL	EXCL	EXCL	IRR

A2	consequences→Add(#)					"Perform read-across to the solute formed. Aging of particles in soil prior to testing is recommended."	"Transformed NF which must be tested against all hypo-theses. Aging of particles in soil prior to testing is recommended."	"NF is gradually dissolving."	"NF is persistent."	
		R1	R2	R3	R4	R5	R6	R7	R8	R9

function 'E-S-2a'.EndpointQualifiers(tl :: TierLevel): EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
A2		
		R1

Class 'E-S-2b' is kind of 'E-S-2'

Hypothesis E-S-2b: NFs that partially dissolve in soil: Following soil exposure fate is driven by dissolution rather than mobility of the NFs. Hazard will be driven by the contribution of solutes and particles to the overall toxicity of the exposure.

Defined expressions

name	type	expression	comment
title	: String	"Hypothesis E-S-2b"	
description	: String	"NFs that partially dissolve in soil: Following soil exposure fate is driven by dissolution rather than mobility of the NFs. Hazard will be driven by the contribution of solutes and particles to the overall toxicity of the exposure."	

Operators

function 'E-S-2b'.DeriveOutcome() : HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment						ELSE
C2	targ_NF	nil	ELSE					-
C3	env_compartment as Soil | soil	-	nil	ELSE				-
C4	medium_interaction.DN_dissolution_in_medium_outcome	-	-	?	instantaneously,quick	gradual	very_slow	-
A1	**begin** outcome := #; result := outcome **end**	IRR	IRR	MI	EXCL	INCL	EXCL	IRR
A2	consequences→Add(#)				"NF is quickly dissolving."	"Aging of NF may be considered prior to exposure."	"NF is persistent."	
A3	consequences→Add(#)					"For read-across to a specific ecotoxicity endpoint the ratio of toxicity of particles to solutes should be considered under the test conditions."		
		R1	R2	R3	R4	R5	R6	R7

function 'E-S-2b'.EndpointQualifiers(tl :: TierLevel) : EPQs [specialization]

C1		-
A1	result := DN_Dissolution_Info(tl).epqs	X
		R1

Class 'TRANSPORT' is kind of EnvHypothesis

Well defined hypothesis classes as described in deliverable D4.1+5.1_RIVM_Final.pdf

Attributes

name	type	domain	inference	comment
transport_likely	:: YesNo			

Defined expressions

name	type	expression	comment
title	: String	"TRANSPORT"	
lead	: String	"TW"	
description	: String	"Transport (advection) of the target material is possible.."	
tiered	: Boolean	False	

Operators

function 'TRANSPORT'.DeriveOutcome(): HypothesisOutcome [specialization]

C1	scenario_type	stEnvironment					ELSE
C2	transport_likely	?	Yes		No	ELSE	-
C3	self~switch_contexts→Select(rel | rel.action = coTransportProcess) | rels	-	0	ELSE	-	-	-

A1	**begin**
	  outcome := #;
	  result := outcome
	end
		MI	MI	INCL	EXCL	MI	IRR

		R1	R2	R3	R4	R5	R6

Class DN_Info

DN_Info contains the relevant information of a decision node at a certain tier level.
It contains guidance texts to present to the user, like an introduction, preferred methods, guidance on assay selection, guidance on when to escalate to a higher tier level.
And finally it also contains, the endpoint qualifiers to express the potential required data to base the outcome of the decsion node upon.
A DN_Info object is a temporary object resulting from hypothesis owned functions ending with _Info().

Attributes

name	type	domain	inference	comment
intro	: String			
epqs	: EPQs			
preferred_methods	: String			
guidance_for_assay_selection	: String			
tier_escalation	: String			

2.3 Defined associations

Association 'hypothesis_context - material'

Association used to assign a 'material' to the context for evaluation of the IATAs.

- zero or more context_1 of HypothesesContext
- exactly one material of any kind of Material

Association 'hypothesis_context - eco_medium'

Association used to assign a potential 'environmental medium' to the context for evaluation of the environmental IATAs.

- zero or more context_2 of HypothesesContext
- at most one external_medium of any kind of EnvMedium

Association switch_cause

Association used to connect the original context with the 'newly' introduced contexts due to context switches. This allows describing a sequence of consecutive context switches. (eg. transport→dissolution→transformation→settling etc.)
Each association also contains an attribute describing the cause of the context switch.

- zero or more switch_contexts of HypothesesContext
- zero or more initiating_hypotheses of any kind of Hypothesis

Attributes

name	type	domain	inference	comment
action	:: ContextSwitchReason			*The action causing the context switch.*

Association `'candidate-scenario'`

Used to relate a candidate nanoform to the different candidate scenarios for grouping.

- one or more nf_scenarios of CandidateScenario
- exactly one candidate of Nanoform

Association `'cs_scenario-contributing_scenario'`

In case of a CS grouping scenario: Used to assign the contributing scenario (part of the exposure scenario and related to the contributing activity) to the grouping scenario object. This allows the grouping scenario to use information contained in the use description of the candidate nanoforms.

- at most one sc_scenario of CS_scenario
- exactly one contributing_scenario of ContributingScenario

Association `'env_scenario-env_medium'`

In case of an ENV_scenario: Used to assign an environmental medium (part of the zone and environmental compartment) to the grouping scenario object. This allows the grouping scenario to use information contained in the environmental compartment description.

- at most one env_scenario of ENV_scenario
- exactly one env_medium of any kind of EnvMedium

Association `'similar_sourcematerial'`

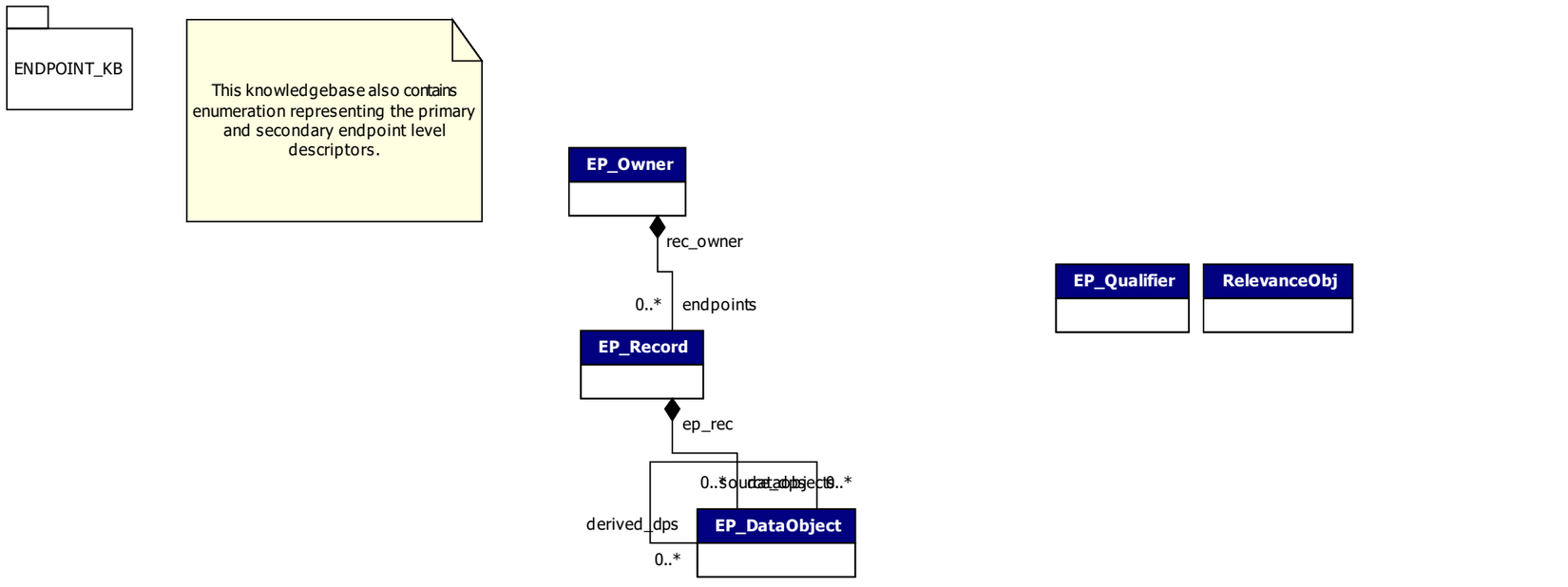
Allows the user to indicate which source_material is found to be the most similar/appropriate for the purpose of read-across of the target material under assessment in the hypothesis and the selected source material.

- zero or more candidate_hypotheses of any kind of Hypothesis
- at most one source_material of any kind of Material

2.4 Defined collections

Hypotheses `defines a sequence containing any kind of` `Hypothesis` `objects.`
GroupDescriptors `defines a sequence containing` `GroupDescriptor` `enumerates.`
GroupingScenarioClasses `defines a sequence containing any kind of` `GroupingScenario` `types.`
SwitchCauses `defines a sequence containing` `switch_cause` `.`
HypothesesClasses `defines a sequence containing any kind of` `Hypothesis` `types.`
HypothesesContexts `defines a sequence containing` `HypothesesContext` `objects.`

Chapter 3 ENDPOINT_KB



The endpoint knowledgebase describes an abstract endpoint owner class EP_Owner which may own endpoint records. An endpoint record is composed of dataobjects belonging to a specific endpoint descriptor. Endpoint descriptors are organised as a set of enumerations representing the endpoint category (aligned with the OECD Harmonised Template level as much as possible). Each endpoint category defines the actual data related result/effect endpoint. The knowledgebase contains a large set of identified endpoints for physchem, environmental fate, human health and ecotoxicity. Endpoint metadata such as value type, units, domain constraints etc. are provided by a series of functions.

3.1 Defined enumerations

PC_IDENTITY

Identifying endpoints

- ID_CAS_REG_NR
- ID_EC_REG_NR
- ID_CHEMICAL_NAME
- ID_IUPAC_NAME

- ID_JRC_ID
  The numbering system for the JRC Representative Nanomaterials stored in the JRC Repository has been revised in order to accommodate more nanomaterials and continue to ensure a high level of traceability. Nanomaterials in the JRC Repository are now identified by the following alphanumeric code (JRC ID): JRCNMXXXYYa, where XXXYY is a number that is unique to a single nanomaterial. This alphanumeric code (first column in the table) shall be used in publications to refer to the nanomaterials that have been issued by the JRC Repository. JRCPDZZZKKa is the code used to indicate the pure dispersant (without nanoparticles) in case of nanomaterials provided as dispersion.
- ID_SMILES
- ID_INCHIKEY
  InChIKey
- ID_INCHI
  InChI
- ID_EINECS

PC_CLASSIFICATION_LABELING

- CLP_HCODE
  HCODE
- CLP_HCODE_GENERIC_CONC_LIMIT
- CLP_HCODE_SPECIFIC_CONC_LIMIT
- CLP_HCODE_M_FACTOR
- GHS_CODE

PC_COMPOSITION

IUCLID : Composition
OHT : Not part of OECD Harmonised Templates
A Substance is defined by its composition. The composition of a Substance can consist of constituents, impurities and additives. This section is a repeatable block section. It enables to enter multiple compositions for a Substance, e.g. to allow different profiles of impurities provided it does not change the identification of the Substance. For detailed instructions on how to define the substance composition in IUCLID, see chapter D.4.1 Substance (create and update substance related information)

- EP_CONSTITUENT_ROLE
  Indicates the specific role/profile of this constituent in the substance as defined by MATERIAL_KB::ConstituentRole
- EP_COMPOSITION_CATEGORY
  Indicates to which composition category the substance or constituent belongs: 'organic compound' ,'organic matter', 'inorganic compound', 'inorganic matter', 'hybrid material', 'mixture', 'water'
- EP_MASS_CONC
  The typical mass concentration of the constituent under consideration within the entire material (sample). [mg/kg]
- EP_MOLECULAR_FORMULA
  An expression which states the number and type of atoms present in a molecule of a substance.
- EP_PURITY
  Degree of purity (%) (REACH regulation, consolidated version 01.01.2020)
- EP_ELEMENTAL_COMPOSITION_MASS_CONC
  Elemental composition expressed as mass concentration.
- EP_ELEMENTAL_COMPOSITION_ATOM_PERC
  Elemental composition expressed as atomic percentage (at%)
- EP_OXIDATION_DEGREE
  Oxidation degree (C/O ratio), ratio between Carbon and Oxygen molucules in graphene oxide

PC_APPEARANCE

IUCLID 4.1: Appearance
OHT 1 : Appearance/physical state/colour

- EP_PHYSICAL_STATE
  Physical state at 20°C and 1013 hPa, enumeration with domain MATERIAL_KB::PhysicalState{gas', 'liquid', 'solid'}
- EP_FORM
  Enumerate like '{solid: particulate/powder'}
- EP_ODOUR
  Enumeration with domain MATERIAL_KB::OdourCategory{'ammonia-like', 'biting', 'characteristic of sulfur-containing compounds', 'characteristic of aromatic compounds', 'faint', 'garlic-like', 'odourless', 'pungent', 'slight', 'sweetish', 'other'}
- EP_COLOUR
  Open text for now..??
- EP_COLOUR_INTENTSITY
  Enumerate: {dark,.. TBD} see registration dossier ECHA

PC_MELTING

IUCLID 4.2: Melting point/ freezing point
OHT 2: Melting point/freezing point

- EP_MELTING_POINT
  The melting point is defined as the temperature at which the phase transition from the solid to the liquid state at atmospheric pressure takes place. (OECD TG 102, 1995)

PC_BOILING

IUCLID 4.3: Boiling point
OHT 3: Boiling point

- EP_BOILING_POINT
  Point at which the vapour pressure of a liquid equals the external pressure acting on the surface of liquid [SOURCE: ISO 11504:2012]
  The normal boiling point of a liquid is defined as the temperature at which the vapour pressure equals the standard atmospheric pressure 101.325 kPa. (OECD TG 103, 1995)

PC_DENSITY

IUCLID 4.4: Density
OHT 4: Density

- EP_TRUE_DENSITY
  The mass of a particle divided by its volume, excluding open pores and closed pores (BSI).
  True density also used for liquids and gases.
- EP_ABSOLUTE_POWDER_DENSITY
  The mass of powder per unit of absolute volume (BSI). Absolute powder volume: (also called Absolute volume): The volume of the solid matter after exclusion of all the spaces (pores and voids) (BSI).
  The mass of powder per volume of solid matter after exclusion of all spaces (pores and voids)
- EP_APPARENT_PARTICLE_DENSITY
  The mass of a particle divided by its apparent (particle) volume (BSI). Apparent particle volume: The total volume of the particle, excluding open pores, but including closed pores (BSI).
  The mass of a particle divided by the total volume of the particle, excluding open pores, but including closed pores.
  According to WP3: Apparent particle density EQUALS Skeletal density! (we could decide to delete apparent this one and always use skeletal density)
- EP_APPARENT_POWDER_DENSITY
  The mass of a powder divided by its apparent volume (BSI). Apparent powder volume: The total volume of solid matter, open pores and closed pores and interstices (BSI).
  The mass of a powder divided by the total volume of solid matter, open pores and closed pores and interstices.
- EP_BULK_DENSITY
  Bulk density: (also called Bulk powder density):
  The apparent powder density under defined conditions (BSI).
  The mass of the particles divided by the volume they occupy that includes the space between the particles (ASTM D5004).
  The ratio of the mass of a collection of discrete pieces of solid material to the sum of the volumes of: the solids in each piece, the voids within the pieces, and the voids among the pieces of the particular collection (ASTM D3766).
  for solids only (IUCLID source)
  The density of a solid is derived from the difference in weight between a sample in air and in a liquid of known density (e.g. water). The density thus measured is only representative of the particular sample employed (bulk density). (OECD TG 109, 2012)
- EP_EFFECTIVE_DENSITY
  The effective density of nano-agglomerates in liquid suspension refers to the density of the agglomerate unit, which includes both particles and media components, as opposed to the density of the primary particle, which is simply the density of the raw ENM material
  (particle effective density) ENM_0000093
  Effective particle density: The mass of a particle divided by its volume including open pores and closed pores (BSI).
- EP_ENVELOPE_DENSITY
  The ratio of the mass of a particle to the sum of the volumes of: the solid in each piece and the voids within each piece, that is, within close-fitting imaginary envelopes completely surrounding each piece (ASTM D3766).
- EP_SKELETAL_DENSITY
  The ratio of the mass of discrete pieces of solid material to the sum of the volumes of: the solid material in the pieces and closed (or blind) pores within the pieces (ASTM D3766).
  Ratio of sample mass to skeleton volume (ISO 15901-1:2016, skeleton density)
  Skeleton volume: volume of the sample including the volume of closed pores (if present) but excluding the volumes of open spores as well as that of void spaces between particles within the bulk sample (ISO 15901-1:2016, source: ISO 12514)
- EP_TAP_DENSITY
  The apparent powder density obtained under stated conditions of tapping (BSI).
  Nanoreg D2_03 Tap density describes the mass per volume after powder compaction in a cylinder (50 times repeated 25 mm drop of a cylinder onto a rubber pad) or by the use of a Dry Substance Jolting Volumeter (ISO 787).
  A known weight of a solid material is placed in a glass graduated (i.e. measuring) cylinder and its volume measured to determine the 'pour density.' The cylinder is then raised and allowed to fall vertically through a distance of 25 mm on a rubber pad 50 times (or this may be performed using a Dry Substance Jolting Volumeter as described in ISO 787/11). The volume is measured again to determine the 'tap density.' (OECD TG 109, 2012)
- EP_THEORETICAL_DENSITY
  The ratio of the mass of a collection of discrete pieces of solid material to the sum of the volumes of said pieces, the solid material having an ideal regular arrangement at the atomic level (ASTM).
  Theoretical density is true density of a material corresponding to the limit attainable through full density products without pores. (https://www.sciencedirect.com/topics/engineering/theoretical-density)
- EP_RELATIVE_DENSITY
  Relative density is the ratio of the density (mass of a unit volume) of a substance to the density of a given reference material.
  (dimensionless unit)
  The relative density (D20/4, density at 20 degrees Centigrade relative to water at 4 degrees Centigrade) may be used to compare different chemicals. (OECD TG 109, 2012)

PC_GRANULOMETRY

IUCLID 4.5 Particle size distribution (Granulometry)
OHT 5: Particle size distribution (Granulometry)/Fibre length and diameter distribution
A typical order of length scale is: largest dimension > hydrodynamic diameter > volume (or mass) equivalent diameter > Stokes diameter > VSSA equivalent diameter > smallest dimension (Appendix 4).

- EP_NOMINAL_DIAMETER
  The indicative particle diameter as provided by the supplier
- EP_NOMINAL_LENGTH
  The indicative particle length as provided by the supplier / manufacturer
- EP_PRIMARY_PARTICLE_DIAMETER
  primary particle: original source particle (3.1) of agglomerates (3.4) or aggregates (3.5) or mixtures of the two [SOURCE: ISO 26824:2013, 1.4] (ISO/TS 80004-2:2015)
  Primary particles are the original seeds from which particles grow and are therefore an unrelated concept to constituent particles, aggregates and agglomerates.
  Therefore, the term 'primary particle' is irrelevant for the EC NM definition. (JRC Report 2019, An overview of concepts and terms used in the European Commission's definition of nanomaterial)
- EP_PRIMARY_PARTICLE_LENGTH
- EP_CONSTITUENT_PARTICLE_SIZE
  (JRC Report 2019, An overview of concepts and terms used in the European Commission's definition of nanomaterial)
- EP_FERET_DIAMETER_D1
  Feret's diameter D1 (minimum distance edge to edge, the minor axis). Minimum diameter D1 corresponds to the "breadth" of the particle. [ISO 9276-6:2008 8.1.2]
  In case of agglomerates/aggregates the minimum Feret diameter (EP_FERET_DIAMETER_D1) refers to the entire agglomerate/aggregate, whereas the maximum inscribed circle (EP_LARGEST_INTERNAL_CIRCLE) does not refer to the entire aggregate, but to the constituent particles of the agglomerate/aggregate (from the NanoDefine project [21]).
- EP_FERET_DIAMETER_D3
  Feret's diameter D3 (maximum distance edge to edge, the major axis), Maximum diameter D3 corresponds to the "length" of the particle; [ISO 9276-6:2008 8.1.2]
- EP_LARGEST_INTERNAL_CIRCLE
  Largest internal circle or maximum inscribed circle diameter: it is the diameter of the largest circle that fits inside the virtual envelope of the boundaries of the particle on a 2D image.
  In case of agglomerates/aggregates the minimum Feret diameter (EP_FERET_DIAMETER_D1) refers to the entire agglomerate/aggregate, whereas the maximum inscribed circle does not refer to the entire aggregate, but to the constituent particles of the agglomerate/aggregate (from the NanoDefine project [21]).
- EP_LEGENDRE_ELLIPSE_D1
  Legendre ellipse D1, (length of the minor axis of the legendre ellipse)
  An ellipse with its centre at the particle's centroid and with the same geometrical moments, up to the second order, as the original particle area. [ISO 9276-6:2008 8.1.2]
- EP_LEGENDRE_ELLIPSE_D3
  Legendre ellipse D3, (length of the major axis of the legendre ellipse)
  An ellipse with its centre at the particle's centroid and with the same geometrical moments, up to the second order, as the original particle area. [ISO 9276-6:2008 8.1.2]
- EP_GEODESIC_LENGTH_D3
  Geometrical descriptor, length of the fibre when stretch into a straight line. Provide definition [ISO 9276-6:2008]
- EP_GEODESIC_THICKNESS
  Is the thickness of the individual fibre, and therefore ≤ as the EP_FERET_DIAMETER_D1
  Provide definition [ISO 9276-6:2008]
- EP_EQUIVALENT_CIRCLE_DIAMETER
  *Diameter of a sphere having the same projection area as the particle: SQRT(4 * [Area] / π) (Also used: equivalent circle diameter, ECD) [ISO 9276-6:2008 7]*
- EP_SURFACE_EQ_SPHERE_DIAMETER
  D_surface = diameter of a sphere with the same surface as the particle
- EP_VOLUME_EQ_SPHERE_DIAMETER
  D_volume = diameter of a sphere with the same volume as the particle (Equivalent volume diameter)
- EP_VOLUME_EQ_DISC_DIAMETER
  Diameter of a disc with the same volume as the disc/platelett like particle.
- EP_VOLUME_EQ_DISC_THICKNESS
  Thickness of a disc with the same volume as the disc/platelett like particle.
- EP_VOLUME_EQ_CYLINDER_DIAMETER
  diameter of a cylinder with the same volume as the fibre like particle.
- EP_VOLUME_EQ_CYLINDER_LENGTH
  Length of a cylinder with the same volume as the fibre like particle.
- EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER
  Hydrodynamic equivalent diameter D_hydro (= diameter of a sphere with the same translational diffusion coefficient as the particle in the same fluid under the same conditions)
  equivalent spherical diameter of a particle in a liquid having the same diffusion coefficient as the real particle in that liquid [SOURCE: ISO/TS 80004□6:2013, 3.2.6]
- EP_Z_AVERAGE_DIAMETER
  The Z-Average size or Z-Average mean used in dynamic light scattering is a parameter also known as the cumulants mean. It is the primary and most stable parameter produced by the technique. The Z-Average mean is the best value to report when used in a quality control setting as it is defined in ISO 13321 and more recently ISO 22412 which defines this mean as the harmonic intensity averaged particle diameter.
  Z-average size is the intensity weighted harmonic mean size
  The intensity-weighted mean diameter derived from the cumulants analysis
  Intensity weighted hydrodynamic diameter. Z-AVE HYDRODYNAMIC DIAMETER (DLS RESULT)
- EP_INTENSITY_WEIGHTED_SIZE
  Intensity weighted particle size, used to report size in methods that measure large number of particles like DLS, SAXS etc. The Z-average is derived from these results?
- EP_STOKES_EQ_SPHERE_DIAMETER
  D_Stokes (= equivalent diameter corresponding to the diameter of a sphere with the same final settling velocity as the particle undergoing laminar flow in a fluid of the same density and viscosity)

- EP_AERODYNAMIC_EQ_SPHERE_DIAMETER
  The diameter in [nm] of an equivalent spherical particle with unit density and the same settling velocity in air as the particle under consideration.
  The aerodynamic diameter of an irregular particle is defined as the diameter of the spherical particle with a density of 1000 kg/m3 and the same settling velocity as the irregular particle. (Wikipedia)
  The diameter of a sphere with unit density that has aerodynamic behavior identical to that of the particle in question; an expression of aerodynamic behavior of an irregularly shaped particle in terms of the diameter of an idealized particle. Particles having the same aerodynamic diameter may have different dimensions and shapes.
  [https://www.opentoxipedia.org/index.php/Aerodynamic_diameter]
  [constraint, only relevant if medium.physical_state = gas]
  The median aerodynamic diameter => MAD
- EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER
  Mass Median Aerodynamic Diameter (MMAD) is defined as the aerodynamic diameter [EP_AERODYNAMIC_EQ_SPHERE_DIAMETER] at which 50% of the particles by mass are larger and 50% are smaller.
- EP_SIEVE_EQ_SPHERE_DIAMETER
  Sieve D (= equivalent diameter corresponding to the diameter of a sphere passing through a sieve of defined mesh size with square or circular apertures).
- EP_ELECTRICAL_MOBILITY_EQ_SPHERE_DIAMETER
  Electrical mobility equivalent diameter, defines the size of charged particles with the same electrical mobility or the same terminal migration velocity in still air under the influence of a constant electrical field. [ISO 27891:2015 3.16]
  ES-DMA result
- EP_DISPERSITY
  This index is a number calculated from a simple 2 parameter fi t to the correlation data (the cumulants analysis). The dispersity (PDI) is dimensionless and scaled such that values smaller than 0.05 are rarely seen other than with highly monodisperse standards. Values greater than 0.7 indicate that the sample has a very broad size distribution and is probably not suitable for the dynamic light scattering (DLS) technique. The various size distribution algorithms work with data that falls between these two extremes. The calculations for these parameters are defined in the ISO standard document 13321:1996 E and ISO 22412:2008.
- EP_DISPERSITY_2
  PDI defined as D(w)/D(n), where D(w) is the mean particle size expressed in a weight basis while D(n) is the mean particle size expressed in a number basis. (CLS)
- EP_MODE_COUNT
  The number of intensity peaks dectected. (PEAK = MODE) (ThinkWorks) Perhaps extend this descriptor like EP_INTENSITY_MODE_COUNT
- EP_FULL_WIDTH_AT_HALF_MAXIMUM
  The same as HALF HEIGHT PEAK WIDTH??
- EP_RADIUS_OF_GYRATION
  RADIUS OF GYRATION (SAXS)
- EP_GEOMETRIC_MEAN_DIAMETER
  Is this a relevant endpoint descriptor it seams to lack an indication of the base.. number, mass, volume, surface etc??
- EP_DERIVED_COUNT_RATE
  DLS specific (The amount of protons arriving at the detector per second) is expresses in Kcps (Kilo counts per second, which is equivalent to 1000 photons ariving at the detector per second.)
  Perhaps make descriptor more specific.. EP_DERIVED_PHOTON_COUNT_RATE??
- EP_RELATIVE_INTENSITY
  DLS specific?? PERHAPS RENAME in EP_RELATIVE_SCATTERING_INTENSITY
- EP_DIMENSION
  Represent the dimension a size is related to. D1, D2 and D3 where D1 is the smallest, D2 is the intermediate and D3 the largest dimension.
- EP_OBSERVATION_SCALE
  ISO/TS 11888:2017(E)
  atomic scale
  Mesoscopic (individual)
  “macroscopic” describes the shape and size of MWCNT aggregates or agglomerates
- EP_DmPx_D1
  DmPx_D1, X% of the populations mass lies below this size of the smallest dimension.
- EP_DmPx_D2
  DmPx_D2, X% of the populations mass lies below this size of the 2nd dimension.
- EP_DmPx_D3
  DmPx_D3, X% of the populations mass lies below this size of the largest dimension.
- EP_DnPx_D1
  DnPx_D1 of particle level , X% of the populations number lies below this size of the smallest dimension.
- EP_DnPx_D2
  DnPx_D2, X% of the populations number lies below this size of the second dimension.
- EP_DnPx_D3
  DnPx_D3, X% of the populations number lies below this size of the largest dimension.
- EP_DvPx_D1
  DvPx_D1, X% of the populations volume lies below this size of the smallest dimension.
- EP_DvPx_D2
  DvPx_D2, X% of the populations volume lies below this size of the second dimension.
- EP_DvPx_D3
  DvPx_D3, X% of the populations volume lies below this size of the largest dimension.
- EP_DsPx_D1
  DsPx_D1, X% of the populations surface area lies below this size of the smallest dimension.
- EP_DsPx_D2
  DsPx_D2, X% of the populations surface area lies below this size of the second dimension.
- EP_DsPx_D3
  DsPx_D3, X% of the populations surface area lies below this size of the largest dimension.

- EP_DiPx_D1
  DiPx_D1, X% of the populations light intensity lies below this size of the smallest dimension.
- EP_DiPx_D2
  DiPx_D2, X% of the populations light intensity lies below this size of the second dimension.
- EP_DiPx_D3
  DiPx_D3, X% of the populations light intensity lies below this size of the largest dimension.

PC_VAPOUR

IUCLID 4.6: Vapour pressure
OHT 6: Vapour pressure

- EP_VAPOUR_PRESSURE
  The vapour pressure of a substance is defined as the saturation pressure above a solid or liquid substance. The SI unit of pressure, which is the pascal (Pa), should be used. (OECD TG 104, 2006)

PC_PARTITION

IUCLID 4.7 : Partition coefficient
OHT 7: Partition coefficient

- EP_LOG_POW
  The partition coefficient between water and 1-octanol (POW) is defined as the ratio of the equilibrium concentrations of the test substance in 1-octanol saturated with water (CO) and water saturated with 1-octanol (CW).
  POW = CO / CW
  As a ratio of concentrations it is dimensionless. Most frequently it is given as the logarithm to the base 10 (log POW). POW is temperature dependent and reported data should include the temperature of the measurement. (OECD TG 123, 2006)
- EP_LOG_K_VALUE
  ??
- EP_CONC_IN_WATER
- EP_CONC_IN_OCTANOL

PC_WATER_SOL

IUCLID 4.8: Water solubility
OHT 8: Water solubility

- EP_WATER_SOL
  The water solubility of a substance is the saturation mass concentration of the substance in water at a given temperature. Water solubility is expressed in mass of solute per volume of solution. The SI unit is kg/m3 but g/l is commonly used. (OECD TG 105, 1995)
- EP_DISSOLUTION_RATE
  The amount of substance dissolved (solute) into a solvent over time, expressed as ng/cm2/h
- EP_DISSOLUTION_HALF_TIME
  Dissolution expressed as the time needed to dissolve half the mass.
- EP_DISSOLUTION_MASS_LOSS
  The mass percentage of substance dissolved (solute) into a solvent per hour (expressed as %/h) (based on dissolution rate definition in OECD Guidance Documents 317 & 318).
- EP_INTRACELLULAR_DISSOLUTION_RATE
  %
- EP_INTRACELLULAR_DISSOLUTION_HALF_TIME
  H-I-1, H-I-2 => Qualitiative outcome
- EP_INTRACELLULAR_DISSOLUTION_MASS_LOSS
- EP_TRANSFORMATION_D1
  % change in morphology of the smallest dimension, pre versus post incubation transformation.
  (reduction in size D1?)
- EP_TRANSFORMATION_D3
  % change in morphology of the largest dimension, pre versus post incubation transformation.
  (reduction in size D3?)
- EP_TRANSFORMATION_MORPHOLOGY
  % of ??
- EP_SOLUBILITY
  The solubility of a substance in a given media is the saturation mass concentration of the substance in that given solvant at a given temperature. The solubility is expressed in mass of solute per volume of solution. The SI unit is kg/m3 but g/l is commonly used.(OECD Guidline 105)
  The quantity of solute that dissolves in a given quantity of solvent to form a saturated solution (OECD Guidance Documents 317 & 318)
  However, unit ppm is used in IATA.
- EP_PERCENTAGE_DISSOLVED

PC_SOL_ORGANIC

IUCLID 4.9: Solubility in organic solvents
OHT 9: Solubility in organic solvents/fat solubility

- EP_SOL_ORGANIC
  The mass fraction of a substance which forms a homogeneous phase with a liquid fat(oil) without giving rise to chemical reactions is defined as fat solubility. The maximum of such mass fraction is called the saturation mass fraction, and this is a function of temperature. The composition of fats will differ from organism to organism and even within a single organism. Since it is desirable to be able to compare results from different laboratories, it is necessary to employ standard fat. This standard fat should be similar in composition and behaviour to materials occurring naturally, and a commercial triglyceride mixture described in the Annex satisfies this requirement, although any other mixtures of triglycerides that give demonstrably comparable results can be used. The saturation mass fraction of a substance should be given in g/kg of standard fat and referenced to 37°C ± 0.5°C. (OECD TG 116, 1981)

PC_SURFACE_TENSION

IUCLID 4.10: Surface tension
OHT 10: Surface tension

- EP_WATER_CONTACT_ANGLE
  When a liquid does not spread on a substrate (usually a solid), a contact angle (ϑ) is formed which is defined as the angle between two of the interfaces at the three-phase line of contact. It must always be stated which interfaces are used to define ϑ. It is often necessary to distinguish between the 'advancing contact angle' (ϑa), the 'receding contact angle' (ϑr) and the 'equilibrium contact angle' (ϑe). (IUPAC Gold Book, https://goldbook.iupac.org/terms/view/C01290)

PC_STABILITY_THERMAL_SUNLIGHT_METALS

IUCLID 4.19: Stability: thermal, sunlight, metals
OHT 19: Stability: thermal, sunlight, metals

- EP_MASS_LOSS
  Thermogravimetric analysis (TGA) is conducted on an instrument referred to as a thermogravimetric analyzer. A thermogravimetric analyzer continuously measures mass while the temperature of a sample is changed over time. Mass, temperature, and time in thermogravimetric analysis are considered base measurements while many additional measures may be derived from these three base measurements.
  TGA provide thus the weight loss [%] or mass loss [g] (of the organic matter) as a function of temperature.
- EP_MASS_LOSS_WATER

PC_NON_SATURATED_PH

IUCLID 4.20: pH
OHT 20: pH

- EP_PH
  pH is defined as the decimal logarithm of the reciprocal of the hydrogen ion activity in a solution.(Covington, A. K.; Bates, R. G.; Durst, R. A. (1985). "Definitions of pH scales, standard reference values, measurement of pH, and related terminology" (PDF). Pure Appl. Chem. 57 (3): 531–542. doi:10.1351/pac198557030531.) OECD 122 (Test Guideline) Electrometric determination of pH measures the negative log10 aqueous hydronium ion concentration of ideal solutions. Dimensionless quantity.

PC_DISSOCIATION

IUCLID 4.21: Dissociation constant
OHT 21: Stability: Dissociation constant
OECD GD 112: Dissociation is the reversible splitting into two or more chemical species which may be ionic. The process is indicated generally by: RX ⍰ R+ + X- and the concentration equilibrium constant governing the reaction is K= [R+][X-]/[RX]

PC_VISCOSITY

IUCLID 4.22: Viscosity
OHT 22: Viscosity

- EP_VISCOSITY
  OECD GD 114: Viscosity is the property of a fluid substance of absorbing a stress during deformation which depends on the rate of the deformation. Similarly, the stress can be regarded as the cause which brings about a deformation rate. The shear stress τ and the shear rate D are related by the equation: τ= η D. η is defined as the dynamic viscosity. The SI unit of dynamic viscosity is the Pascal second, [Pa s]. The SI unit of kinematic viscosity (dynamic viscosity divided by the density of the fluid) is the square metre per second, [m2/s].

PC_AGGLOMERATION_AGGREGATION

IUCLID 4.24: Agglomeration/aggregation
OHT 101: Nanomaterial agglomeration/aggregation
OECD TG318: Process of contact and adhesion whereby dispersed particles are held together by weak physical interactions ultimately leading to enhanced sedimentation by the formation of precipitates of larger than colloidal size (agglomerates) (slightly modified according to 7). In contrast to aggregation where particles held by strong bonds like sinter bridges, agglomeration is a reversible process.

- EP_AA_INDEX
  The agglomeration/aggregation index is a unitless quantity. It is here defined as 1– A'/A", where A' is the mean diameter of primary particles and A" is the mean diameter of aggregates. (source OHT)

- EP_AA_RATIO
  The agglomeration/aggregation ratio is a unitless quantity. It is the ratio of the number of agglomerates to single particles.
- EP_FRACTAL_DIMENSION
  Fractal Dimension (DF) is the power that an equivalent radius of a NP agglomerate scales to in order to scale to its mass. A DF of 3 hence corresponds to a solid sphere (no porosity) and a value of 1 describes a rod. NP agglomerates can be divided into diffusion limited agglomerates (DLCA) with DF values of approximately 1.8, and reaction limited cluster agglomerates (RCLA) with a DF value between 2.1 and 2.5. (SAX, VCM)

PC_CRYSTALLINE_PHASE

IUCLID 4.25: Crystalline phase
OHT 102: Nanomaterial crystalline phase
Crystalline (crystal) phase consist of ordered and periodic atomic arrangements (Nature Reviews Chemistry volume 4, pages243–256(2020)).

- EP_CRYSTALLINITY
  <definition>
  <text>["Crystallinity is defined as the ratio between the mass fraction of crystalline phases versus the total mass (both crystalline phases and amorphous)."]</text>
  <source>["ISO 13779-3:2018 3.14"]</source>
  <ontology/>
  </definition>
- EP_CRYSTAL_SYSTEM
  A material in which the atoms are arranged in a translationally periodic array in the three dimensions or which are arranged in rotationally periodic arrays in three dimensions (Cullity, 1978, Element of X-Ray Diffraction, Second Edition, Addison-Wesley Publishing Co., Reading, MA, 1978). In total there are seven crystal systems: triclinic, monoclinic, orthorhombic, tetragonal, trigonal, hexagonal, and cubic.
- EP_SPACE_GROUP
  A space group is the symmetry group of a configuration in space, usually in three dimensions. In crystallography, space groups are also called the crystallographic or Fedorov groups, and represent a description of the symmetry of the crystal. (Hiller, Howard (1986). "Crystallography and cohomology of groups". Amer. Math. Monthly. 93 (10): 765–779. doi:10.2307/2322930. JSTOR 2322930). Crystals can be classified according to 230 space groups and a space group can be referred to by a number or the space group symbol.
- EP_MINERAL_NAME
  Name of the mineral.

PC_CRYSTALLITE_AND_GRAIN_SIZE

IUCLID 4.26: Crystallite and grain size
OHT 103: Nanomaterial crystallite and grain size
A grain consists of a single material, but may be crystalline, or polycrystalline. An individual crystallite consists of a single phase.

- EP_CRYSTALLITE_SIZE
  Crystallite size is the size of a single crystal in powder form which contains a single phase.
- EP_GRAIN_SIZE
  Grain consists of a single material that may be crystalline or polycrystalline. SI unit for grain size [m].

PC_ASPECT_RATIO_SHAPE

IUCLID 4.27: Aspect ratio/shape
OHT 104: Nanomaterial aspect ratio/shape

- EP_ASPECT_RATIO_D3_D1
  Ratio of maximum D3 to minimum D1 Feret diameter (D3/D1), will result in a value ≥ 1.
  Ratio of length to width of a particle. [ISO 13794:1999 2.10]
- EP_ELLIPSE_RATIO_D3_D1
  The aspect ratio of the particle's fitted ellipse, i.e., [Major Axis]/[Minor Axis]. https://imagej.nih.gov/ij/docs/guide/146-30.html
  PC_GRANULOMETRY::EP_LEGENDRE_ELLIPSE_D3/PC_GRANULOMETRY::EP_LEGENDRE_ELLIPSE_D1
- EP_ASPECT_RATIO_D1_D3
  Ratio of minimum D1 to maximum D3 Feret diameter (D1/D3), will result in a value >0 and ≤ 1. For not very elongated particles. [ISO 9276-6:2008 8.1.3]
- EP_ELLIPSE_RATIO_D1_D3
  PC_GRANULOMETRY::EP_LEGENDRE_ELLIPSE_D1 / PC_GRANULOMETRY::EP_LEGENDRE_ELLIPSE_D3
- EP_COMPACTNESS
  Degree to which the particle (or its projection area) is similar to a circle, considering the overall form of the particle: [ISO 9276-6:2008 8.1.3]
  *Compactness = SQRT(4 * [Area] / π) / [D3 Feret diameter]*
- EP_ROUNDNESS
  Degree to which the particle (or its projection area) is similar to a circle, considering the overall form of the particle: [ISO 9276-6:2008 8.1.3]
  Roundness = (4 × [Area]) / (π × [D3 Feret diameter]^2)

- EP_CIRCULARITY
  Circularity, is defined as the degree to which the particle is similar to a circle, taking into consideration the smoothness of the perimeter. This means circularity is a measurement of both the particle form and roughness. Thus, the further away from a perfectly round, smooth circle a particle becomes, the lower the circularity value. Circularity is a dimensionless value.
  [ISO9276-6 8.2]
  Degree to which the particle (or its projection area) is similar to a circle, considering the smoothness of the perimeter:
  SQRT(4π x [Area] / [Perimeter]^2)
- EP_CIRCULARITY_FORM_FACTOR
  Circularity, equal to 4π × [Area]/[Perimeter]^2 ranges from 0 (infinitely elongated polygon) to 1 (perfect circle). https://imagej.nih.gov/ij/docs/guide/146-30.html
- EP_SOLIDITY
  Solidity, S, is the measurement of the overall concavity of a particle. It is defined as the image area, A, divided by the convex hull area, Ac, as given in Equation 9. Thus, as the particle becomes more solid, the image area and convex hull area approach each other, resulting in a solidity value of one. However, as the particle form digresses from a closed circle, the convex hull area increases and the calculated solidity decreases. Solidity is a dimensionless value.
  [ISO9276-6 8.2]
  Measure of the overall concavity of a particle:
  Solidity = [Area]/ [Ac] where Ac is the area of the convex hull (envelope) bounding the particle
- EP_CONVEXITY
  Convexity, Cx, is a measurement of the particle edge roughness and is defined as the convex hull perimeter, Pc, divided by the actual perimeter, P, as given in Equation 8. Thus, as the surface of the particle becomes rough, the actual perimeter increases, thus lowering the convexity measurement. Convexity is a dimensionless value.

  [ISO9276-6 8.2]
  Convexity Pc / P = where Pc is the length of the perimeter of the convex hull (envelope) bounding the particle []
- EP_DYNAMIC_SHAPE_FACTOR
  Provide definition
- EP_SHAPE_CATEGORY
  Four shape categories: spheriodal, elongated, platelets, mixed
- EP_SHAPE_SUBCATEGORY
  Subcategories of the overall shape category: [Spherical, Pyramidal, Cubic, Star, Orthorhombic, Polyhedral, Tubes, Rods, Discs, Plates]
- EP_ASSEMBLY_STRUCTURE_CP
  The assembly structure of the constituent particle. MATERIAL:KB::AssemblyStructure{ 'shell-like structures', 'multi-walled', 'nano-onions' , 'multi-layers' , 'hollow structures'}
  Warning! Combinations are also possible..
- EP_ASSEMBLY_STRUCTURE_AGG
  The assembly structure of the secondary aggregated particles (agglomeration state): see AssemblyStructure2nd
- EP_NUMBER_OF_LAYERS
  Number of layers or sheets, for instance in graphene oxide nanosheets.
- EP_NUMBER_OF_WALLS
  Number of wall in a multwall nanotube.

PC_SPECIFIC_SURFACE_AREA

IUCLID 4.28: Specific surface area
OHT 105: Nanomaterial specific surface area

- EP_SURFACE_AREA
  extent of available surface area as determined by a given method under stated conditions
  Note 1 to entry: For the purposes of this International Standard, the area includes the external surface of a solid plus the internal surface of its accessible macro-, meso- and micropores.
  [SOURCE: ISO 15901-1:2006[1], 3.25]
  Is this the same as absolute surface area or total surface??
- EP_MASS_SPECIFIC_SURFACE_AREA
  Absolute surface area of the sample divided by sample mass. [ISO/TS 80004-6:2013 3.6.1]
- EP_SBET
  Brunauer, Emmett and Teller (BET), m2/g => the same as EP_MASS_SPECIFIC_SURFACE_AREA
- EP_VOLUME_SPECIFIC_SURFACE_AREA
  Absolute surface area of the sample divided by sample volume. (VSSA) [ISO/TS 80004-6:2013 3.6.1] m2/cm3
  *EP_MASS_EXTERNAL_SURFACE [m2/g] * EP_SKELETAL_DENSITY [g/cm3] => [m2/cm3]*
- EP_MASS_EXTERNAL_SURFACE
  This is the mass based external surface area relative to the total mass, where the external surface area is the total surface area minus the surface area of the micropores.
  See, BET VSSA assay WP3
- EP_VOLUME_EXTERNAL_SURFACE
  This is the volume based external surface area relative to the total volume, where the external surface area is the total surface area minus the surface area of the micropores.
- EP_MASS_MICROPOROSITY_SURFACE
  Surface area of the micropores in the material relative to the total mass. Unit [m2/g].
- EP_TITRATOR_VOLUME
  Volume needed to determine the SSA of a material following the Sears method. Unit [ml].
  See (Sears) expressed in (ml)

- EP_SURFACE_AREA_TO_VOLUME_RATIO
  Surface Area / Volume, a sphere typically has the lowest ratio of all shapes for the same volume.

PC_ZETA_POTENTIAL

IUCLID 4.29: Zeta potential
OHT 106: Nanomaterial Zeta potential

- EP_ZETA_POTENTIAL
  Zeta Potential–electrokinetic potential: the electric potential at the shear plane of the diffuse double layer. The zeta potential is derived from electro-kinetic phenomena, the movement of the particles in an electric field. The conversion of electrophoretic mobility measurements into zeta potential requires several assumptions about the properties of the double layer.As long as the assumptions are always identical, identical conversions and hence zeta potentials are retrieved. Reporting zeta potentials would require the reporting of the assumptions made to make them comparable. [OECD TG 318]
  Unit: [mV]
- EP_ISOELECTRIC_POINT
  IEP –Isoelectric point: the pH at which the zeta potential or particle mobility in response to an electric field is zero. Only in the absence of specifically adsorbing ions which change the surface charge compared to the pristine surface, the IEP equals the point of zero charge (PZC) [OECD TG 318]

PC_SURFACE_CHEMISTRY

IUCLID 4.30: Surface chemistry
OHT 107: Nanomaterial surface chemistry

- EP_ATOMIC_COMPOSITION
  Add to composition..
  Atomic composition of the surface chemistry may refer to hyphenating the TGA (in EP_MASS_LOSS) to evolved gas analysis such as mass spectrometry (TGA-MS). This allows quantitative analysis of the polymer compounds in the material. Another common tool is to hyphenate with FTIR for infra red spectrometry (TGA-FTIR). I am not sure if these come under the same endpoint e.g. EP_EVOLVED_GAS_ANALYSIS or if TGA-MS should be under EP_ATOMIC_COMPOSITION whilst TGA-FTIR should be under EP_COMPOUND_CLASS (or something similar). I ask this because they deliver importantly different results, but in effect give you a quantitative measure of the chemical composition of the polymer. See definitions below for more detail. "TGA-FTIR can be compared to spectral reference databases for identifying the chemical class or family of the unknowns. In many cases, the chemistries can be narrowed down to specific compounds" "TGA-MS provides a sensitive method for analyzing TGA gaseous products in detail... Tentative identification of the original gas products can be performed in two steps: (1) assigning the structure of the fragment ions using the mass data, and, (2) correlating the assigned fragment structures with known fragmentation patterns of specific molecules."definitions from https://www.eag.com/techniques/phys-chem/tga-ega/ as an example.
- EP_MASS_LOSS
  Thermogravimetric analysis (TGA) is conducted on an instrument referred to as a thermogravimetric analyzer. A thermogravimetric analyzer continuously measures mass while the temperature of a sample is changed over time. Mass, temperature, and time in thermogravimetric analysis are considered base measurements while many additional measures may be derived from these three base measurements.
  This is considered part of PC_SURFACE_CHEMISTRY as this technique can be used to measure the % mass loss on heating. This can be used to infer the % mass of coatings in a nanomaterial sample. Example of micro-TGA https://doi.org/10.1021/ac402888v
  Standards for TGA are ASTM E1131, ISO 11358
- EP_NOMINAL_INORGANIC_COMPOSITION
  Text based composition of inorganic elements of surface chemistry
- EP_NOMINAL_ORGANIC_COMPOSITION
  Text based composition of organic elements of surface chemistry

PC_DUSTINESS

IUCLID 4.31: Dustiness
OHT 108: Nanomaterial dustiness
Propensity of materials to produce airborne dust during handling. [ISO 12025:2012 3.2.15]

- EP_RESPIRABLE_DUST_INDEX_MASS
  the mass fraction of inhaled particles penetrating to the unciliated airways
- EP_RESPIRABLE_DUST_INDEX_NUMB
- EP_THORACIC_DUST_INDEX_MASS
  the mass fraction of inhaled particles penetrating beyond the larynx
- EP_THORACIC_DUST_INDEX_NUMB
- EP_INHALABLE_DUST_INDEX_MASS
  the mass fraction of total airborne particles which is inhaled through the nose and mouth.
- EP_INHALABLE_DUST_INDEX_NUMB

PC_AEROSOL_CHARACTERISATION

- EP_AEROSOLISED_PARTICLE_CONC
  The number of particles released due to thermal degradation. (TGA,)

PC_POROSITY

IUCLID 4.32: Porosity
OHT 109: Nanomaterial porosity
Porosity or void fraction is a measure of the void (i.e. 'empty') spaces in a material,and is a fraction of the volume of voids over the total volume.

- EP_VOID_SPACE_FRACTION
  Porosity or void fraction is a measure of the void (i.e. 'empty') spaces in a material,and is a fraction of the volume of voids over the total volume.
- EP_SPECIFIC_PORE_VOLUME
  Volume of open pores unless otherwise stated (ISO 15901-1:2016(en))
- EP_MODAL_PORE_DIAMETER
  Pore diameter of the maximum in a differential pore size distribution curve (ISO 15901-1:2016(en))
- EP_PORE_SIZE
- EP_PORE_RADIUS

PC_POUR_DENSITY

IUCLID 4.33: Pour density
OHT 110: Nanomaterial pour density
IUCLID 5.0 manual
4.34.1.20. Pour density or void fraction is a measure of the void (i.e. 'empty') spaces in a material,and is a fraction of the volume of voids over the total volume.
I DON'T THINK THIS IS THE CORRECT DEFINITION... it is the same as POROSITY definition in IUCLID 5.0.. I guess they mixed up pore and pour!!!
Nanoreg D2_03: Pour density, also called bulk or apparent density, is given by the mass per volume that a given powder occupies as poured directly into a container without any further compaction.

- EP_POUR_DENSITY
  Pour density, also called bulk or apparent density, is given by the mass per volume that a given powder occupies as poured directly into a container without any further compaction.
  Might be equal to PC_DENSITY::EP_APPARENT_POWDER_DENSITY, PC_DENSITY::BULK_DENSITY

  A known weight of a solid material is placed in a glass graduated (i.e. measuring) cylinder and its volume measured to determine the 'pour density.' (OECD TG 109, 2012).

PC_PHOTOCATALYTIC_ACTIVITY

IUCLID 4.34: Photocatalytic activity
OHT 111: Nanomaterial photocatalytic activity

PC_RADICAL_FORMATION_POTENTIAL

IUCLID 4.35: Radical formation potential
OHT 112: Nanomaterial radical/formation potential

- EP_OH_RADICAL_FORMATION_POTENTIAL
  Potential of forming hydroxyl radicals. There appear to be no standardised methods or definitions for this (however, see the OECD document ENV/JM/MONO(2016)7).
- EP_OXIDATIVE_DAMAGE_PER_DOSE
  The oxidative damage / nmol TEU /l.
- EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE
  The nanoform mass based oxidative damage (mBOD) in nmol TUE/mg => Trolox-equivalent units (TEU), Arnaud Gandon et al 2017 J. Phys.: Conf. Ser. 838 012033
- EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE
  The nanoform surface based oxidative damage sBOD in nmol TEU/m2 => Trolox-equivalent units (TEU), Arnaud Gandon et al 2017 J. Phys.: Conf. Ser. 838 012033
- EP_OXIDATIVE_DAMAGE_AUC_MASS
  AUC => Area Under Curve
- EP_OXIDATIVE_DAMAGE_AUC_SURFACE
- EP_SPIN_COUNT_PER_SURFACE_CONC
- EP_SURFACE_REACTIVITY_CPH_DH20_MASS
- EP_SURFACE_REACTIVITY_CPH_DH20_SURF
- EP_SURFACE_REACTIVITY_DMPO_DH20_MASS
  'deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2'
- EP_SURFACE_REACTIVITY_DMPO_DH20_SURF
  'deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2'
- EP_FLUORESCENCE_480_530_AU
  Raw data of DCFH assay, light intensity between wavelength 480-530nm (ex/em 480/530)?? (eNanomapper)
- EP_DCFH_ROS_GENERATION_AU
  Normalised data from [EP_FLUORESCENCE_480_530_AU], DCFH assay (eNanoMapper)
- EP_DCFH_OXIDATION_MASS
- EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL

- EP_DCFH_SCORE_MASS
- EP_DCFH_INTRINSIC_ROS_CHANGE_IN_RFU
  Change in RFU (Relative Fluorescent Unit)
- EP_EPR_SCORE_SURF
- EP_EPR_SCORE_MASS
- EP_EPR_SIGNAL_INTENSITY
- EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL
- EP_FRAS_SCORE_MASS
- EP_FRAS_SCORE_SURF

PC_CATALYTIC_ACTIVITY

IUCLID 4.36: Catalytic activity
OHT 113: Nanomaterial catalytic activity
In the REACH context this seems to be descriptive rather than any specific measurable quantity linked to a specific assay, i.e. any available studies relevant to the catalytic properties of the nanomaterial are summarised.
Increase in the rate of reaction of a specified chemical reaction that an enzyme produces in a specific assay system. (IUPAC Gold Book https://goldbook.iupac.org/terms/view/C00881)

PC_RIGIDITY

Newly introduced Gracious (ThinkWorks)
Rigidity, in the context of this Guidance, is the ability of an elongated particle or platelet to retain its shape, without damage, when subject to mechanical (bending) forces. (ECHA-19-H-14-EN , Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification)

- EP_STATIC_BENDING_PERSISTENCE_LENGTH
  Maximum straight length without static bending (SBPL) (ISO/TS 11888:2017 3.1.4)
- EP_BENDING_RATIO
  Ratio between mean-squared end-to-end distance and squared contour length. (ISO/TS 11888:2017 3.1.8)
- EP_CONTOUR_LENGTH
  Total length of an MWCNT along its axis. (ISO/TS 11888:2017 3.1.5)
- EP_BIOLOGICAL_STIFFNESS
  H-I-1
- EP_YOUNGS_MODULUS
  Young's modulus E describes the material's strain response to uniaxial stress in the direction of this stress (like pulling on the ends of a wire or putting a weight on top of a column, with the wire getting longer and the column losing height),
- EP_SHEAR_MODULUS
  In materials science, shear modulus or modulus of rigidity, denoted by G, or sometimes S or μ, is a measure of the elastic shear stiffness of a material and is defined as the ratio of shear stress to the shear strain.
  The shear modulus G describes the material's response to shear stress (like cutting it with dull scissors).

PC_HYDROPHOBICITY

Newly introduced Gracious (ThinkWorks)
In the Greek words, hydro means water, philicity means affinity, and phobicity means lack of affinity.A surface is hydrophobic when its static water contact angle ϑ is >90° and is hydrophilic when ϑ is <90°. (J. Phys. Chem. Lett. 2014, 5, 4, 686–688)

- EP_WATER_CONTACT_ANGLE
  Perhaps this is already covered in the PC_SURFACE_TENSION category
  Method to measure of wettability (and hydrophobicity thus) of solid surface by water via the Young equation. Unit [°].
  Water contact angle (WCA) is the angle formed tangential to the water droplet at the air–liquid–solid interface. A WCA less than 90 degree is an indication of a wettable surface; a WCA greater than 90 degree indicates poor wettability. (doi.org/10.1016/B978-0-12-802926-8.00002-1)

PC_BIOMOL_INTERACTION

Newly introduced (eNanomapper equivalent BIO_NANO_INTERACTION_SECTION)

- EP_BINDING_ENERGY
- EP_BINDING_ENTHALPY
- EP_BINDING_ENTROPY

EN_PHOTOTRANS_AIR

OHT 24: Phototransformation in air

EN_HYDROLYSIS

OHT 25: Hydrolysis

EN_PHOTOTRANS_WATER

OHT 26: Phototransformation in water

- EP_PHOTOLYSIS_HALF_TIME
  Provide definition..

EN_PHOTOTRANS_SOIL

OHT 27: Phototransformation in soil

- EP_PHOTOLYSIS_HALF_TIME

EN_BIODEG_WATER_SCREEN

OHT 28: Biodegradation in water: screening tests

- EP_PERCENT_BIODEG

EN_BIODEG_WATER_SIM

OHT 29: Biodegradation in water and sediment: simulation tests

- EP_PERCENT_BIODEG

EN_BIODEG_SOIL

OHT 30: Biodegradation in soil => EN_STABILITY_IN_SOIL

- EP_PERCENT_BIODEG

EN_DEGR_MODE_IN_USE

OHT 31: Mode of degradation in actual use

EN_BIOACCU_AQUATIC_SED

OHT 32 Bioaccumulation: aquatic/sediment =>EN_BIOACCUMULATION

- EP_BIOACCUMULATION
  OECD 305, 315, 317

EN_BIOACCU_TERRESTRIAL

OHT 33: Bioaccumulation: terrestrial

EN_ADSORPTION

OHT 34: Adsorption/desorption

EN_HENRY_LAW

OHT 35: Henry's Law constant

EN_DISPERSION_STABILITY_NANOMATERIAL

OHT 401: Dispersion stability of nanomaterials (Version [1.0]-[December 2018])

- EP_DISPERSION_STABILITY
  Dispersion stability refers to the ability of a dispersion to resist change in its properties over time.
  Ability to resist change or variation in the initial properties (state) of a dispersion over time, in other words, the quality of a dispersion in being free from alterations over a given time scale. [ISO 13097:2013]
- EP_BATCH_RETENTION_COEFFICIENT
  Kr batch retention coefficients recommended in D7.4 NanoFASE

EN_BIODURABILITY

Resistance to clearance by chemical and physical means, like resistance to chemical dissolution [ISO/TR 19057]
(Should this be a phychem category endpoint ??)
These endpoints might be moved to the PC_WATER_SOL section (wait for confirmation from WP3)

EC_FISH_TOX_SHORT

OHT 41: Short-term toxicity to fish

- EP_MORTALITY
- EP_DEVELOPMENT
- EP_COAGULATION_OF_FERTILISED_EGGS
- EP_LACK_OF_SOMITE_FORMATION
- EP_LACK_OF_DETACHMENT_OF_TAIL_BUD_FROM_YOLK_SAC
  'lack of detachment of the tail-bud from the yolk sac'
- EP_LACK_OF_HEARTBEAT
- EP_LYSOSOMAL_INTEGRITY
- EP_METABOLIC_ACTIVITY
- EP_PLASMA_MEMBRANE_INTEGRITY

EC_FISH_TOX_CHRONIC

OHT 42: Long-term toxicity to fish

- EP_MORTALITY
- EP_DEVELOPMENT
- EP_GROWTH
  OECD 215
- EP_HATCHING
  OECD 210, 212
- EP_SURVIVAL
- EP_WEIGHT
- EP_LENGTH
- EP_ABNORMAL_APPEARANCE_AND_BEHAVIOR

EC_AQUATIC_INVERT_TOX_SHORT

OHT 43: Short-term toxicity to aquatic invertebrates

- EP_IMMOBILIZATION
- EP_GROWTH
- EP_YIELD
- EP_BIOMASS
- EP_MORTALITY

EC_AQUATIC_INVERT_TOX_CHRONIC

OHT 44: Long-term toxicity to aquatic invertebrates

- EP_REPRODUCTION
- EP_HATCHING
- EP_GROWTH
- EP_IMMOBILIZATION

EC_ALGAE_TOX

OHT 45: Toxicity to aquatic algae and cyanobacteria

- EP_GROWTH
  OECD 201
- EP_BIOMASS
- EP_YIELD

EC_AQ_PLANTS_NONE_ALGAE

OHT 46: Toxicity to aquatic plants other than algae

- EP_GROWTH
  OECD 221
- EP_YIELD

EC_BAC_TOX

OHT 47: Toxicity to microorganisms

- EP_GROWTH_INHIBITION
  -The cell multiplication inhibition for a tested concentration expressed as a percentage. Example of calculation given in ISO 10712 https://www.iso.org/standard/18800.html
  -ECx: Effective concentration for growth inhibition - Concentration of the test sample giving a calculated or interpolated inhibition of cell multiplication compared to that of the control treatment. Example taken from ISO 10712 https://www.iso.org/standard/18800.html
  -NOEC (no observed effect concentration) is the test substance concentration at which no effect is observed. For example, the concentration corresponding to the NOEC, has no statistically significant effect ($p < 0.05$) within a given exposure period when compared with the control.
  -LOEC (lowest observed effect concentration) is the test substance concentration for which the effect is significantly different from control.
- EP_NITRIFICATION_INHIBITION
  LOEC (lowest observed effect concentration) is the lowest test substance concentration for which the effect is significantly different from control. Test method for example ISO 9509:2006 https://www.iso.org/standard/34812.html
- EP_RESPIRATION_INHIBITION
  NOEC (no observed effect concentration) is the test substance concentration at which no effect is observed. In this test, the concentration corresponding to the NOEC, has no statistically significant effect ($p < 0.05$) within a given exposure period when compared with the control. Definition from OECD TG 209
  https://www.oecd-ilibrary.org/environment/test-no-209-activated-sludge-respiration-inhibition-test_9789264070080-en
- EP_OXYGEN_CONSUMPTION
  No observed effect concentration (NOEC) is the test substance concentration at which no effect is observed. Derived from assessment of the inhibitory effect of a test material on the oxygen consumption of microorganisms, for example from ISO 8192:2007 https://www.iso.org/standard/37369.html

EC_SEDIMENT_TOX

OHT 49: Sediment toxicity

- EP_EMERGENCE
  OECD 218,219
- EP_GROWTH
  OECD 219
- EP_SURVIVAL
  OECD 225
- EP_LUMINESCENCE
  E-WS-1c-e (not sure how to use this one.. IC50?)
- EP_REPRODUCTION
- EP_DEVELOPMENT
- EP_DEVELOPMENT_RATE
- EP_SEX_RATIO

EC_SOIL_TOX

OHT 50-1: Toxicity to soil macro-organisms except anthropods

- EP_SURVIVAL
  LC50
- EP_REPRODUCTION
  EC50

EC_TERR_ARTHROP_TOX

OHT 50-2: Toxicity to terrestrial arthropods =>EC_HONEYBEESTOX

- EP_DEVELOPMENT
- EP_EMERGENCE
  OECD 228
- EP_FEMALE_SURVIVOR
  OECD 226
- EP_HATCHING
  OECD 228

EC_TERR_PLANT_TOX

OHT 51: Toxicity to terrestrial plants

- EP_DRY_SHOOT_WEIGHT
  OECD 227
- EP_EMERGENCE
  OECD 208

EC_SOIL_MICRO_TOX

OHT 52: Toxicity to soil microorganisms

EC_BIRDS_TOX

OHT 53: Toxicity to birds

- EP_CRACKED_EGGS
  OECD 206, OPPTS 850.2300
- EP_EGG_PRODUCTION
- EP_EGG_SHELL_THICKNESS
- EP_HATCHABILITY_AND_EFFECTS_ON_YOUNG_BIRDS
  OECD 206

HH_BASIC_TOX

OHT 58: Basic toxicokinetics

- EP_IN_VIVO_ACCUMULATION
  Accumulated dose mg of released ion/kg or particles identification / quantification (see. OECD TG 417)
  Accumulation (Bioaccumulation): Increase of the amount of a substance over time within tissues (usually fatty tissues, following repeated exposure); if the input of a substance into the body is greater than the rate at which it is eliminated, the organism accumulates the substance and toxic concentrations of a substance might be achieved;

HH_DERMAL_ABSORP

OHT 59: Dermal absorption

HH_ACUTE_TOX_ORAL

OHT 60: Acute toxicity: oral

HH_ACUTE_TOX_INHAL

OHT 61: Acute toxicity: inhalation

- EP_TOX_CATEGORY_STIS
  Toxicity category obtained from in vivo STIS assay.

HH_ACUTE_TOX_DERMAL

OHT 62: Acute toxicity: dermal

HH_SKIN_IRRITATION

OHT 64: Skin irritation/corrosion

HH_EYE_IRRITATION

OHT 65: Eye irritation

HH_SKIN_SENSITISATION

OHT 66-1: Skin sensitisation

HH_RESP_SENSITISATION

OHT 66-2: Respiratory sensitisation

HH_REPEATED_ORAL

OHT 67: Repeated dose toxicity: oral

- EP_CELL_NUMBER_IN_BALF
  https://www.rivm.nl/sites/default/files/2019-01/NANoREG_D4_15_DR_Protocol_for_inhalation_exposure_and_choice_of_biological_relevant_endpoints.pdf
- EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF
- EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF
- EP_ALVEOLAR_LYMPHOCYTES_NUMBER_IN_BALF
- EP_ALVEOLAR_EOSINOPHILS_NUMBER_IN_BALF
- EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF
  The percentage of macrophage cells in the BAL fluid.
  different cell types (macrophages, neutrophils, eosinophils) in the BALF
- EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF
  The percentage of neutrophils cells in the BAL fluid.
- EP_ALVEOLAR_LYMPHOCYTES_PERC_IN_BALF
  The percentage of lymphocyte cells in the BAL fluid.
- EP_ALVEOLAR_EOSINOPHILS_PERC_IN_BALF
  The percentage of eosinophil cells in the BAL fluid.

HH_REPEATED_INHAL

OHT 68: Repeated dose toxicity: inhalation

- EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF
- EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF
- EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF
- EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF

HH_REPEATED_DERMAL

OHT 69-1: Repeated dose toxicity: dermal

HH_GENETIC_IN_VITRO

OHT 70: Genetic toxicity in vitro
gene mutation, chromosomal damage (clastogenicity) and numerical chromosomal damage (aneuploidy)?

- EP_DNA_STRAND_BREAKS
- EP_FPG_SENSITIVE_SITES
  FPG-sensitive sites

HH_GENETIC_IN_VIVO

OHT 71: Genetic toxicity in vivo

- EP_DNA_STRAND_BREAKS

HH_LUNG_INSTILLATION

Isn't this the same as EN_BIODURABILITY??
Perhaps also move to PC_WATER_SOL ..

- EP_RETAINED_FIBRE_BURDEN
  Retained burden measured in mg particle / g lung tissue, used to calculate NF half-life
  %
- EP_RETAINED_FIBRE_HALF_TIME
- EP_IN_VIVO_HALF_TIME
- EP_CLEARANCE_RATE
- EP_LUNG_BURDEN_Tx
  Lung burden at time post exposure (T(x)) is recorded as mg per g of lung tissue. Initial lung burden to confirm and compare deposition should be recorded at day 1 post end of exposure (T1)

HH_CYTOTOXICITY

Cytotoxicity (not covered by OHT??)
Treating cells with the cytotoxic compound can result in a variety of cell fates.
ENM_0000068_SECTION

- EP_APOPTOSIS
  The cells can activate a genetic program of controlled cell death (apoptosis).
- EP_NECROSIS
  The cells may undergo necrosis, in which they lose membrane integrity and die rapidly as a result of cell lysis.
- EP_CELL_VIABILITY
  The cells can stop actively growing and dividing (a decrease in cell viability) => ENM_0000068
  number of "healthy" cells within a population
- EP_CELL_PROLIFIRATION
  number of actively dividing cells in a population
- EP_WST_CELL_VIABILITY_ABSORPTION_450_NM
  Absorption of light (450 nm) expressed in AU???
- EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM
  Absorption of light (540 nm) expressed in AU???
- EP_WST_CELL_VIABILITY_ABSORPTION_420_480_NM
  Absorption of light (unit O.D?) Optical density?
- EP_WST_VIABILITY_PERC_OF_CONTROL
- EP_NRU_VIABILITY_PERC_OF_CONTROL
- EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL
- EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL
- EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL
- EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE
- EP_RESAZURIN_VIABILITY_PERC_OF_CONTROL
- EP_NORMALISED_POST_EXPOSURE_CELL_INDEX_1
  Endpoint of Impedance Analysis of Adherent cells (NanoReg data)
- EP_IAAC_CYTOTOXICITY_PERC_OF_CONTROL
  Impedance Analysis Adherent cell line cytotoxicity
- EP_IAAC_CYTOTOXICITY_ICx
- EP_CFE_CYTOTOXICITY_PERC_OF_CONTROL

HH_INFLAMMATION

Inflammation category (not yet covered by OHT, inhalation IATA)

- EP_INFLAMMASOME
  IL-1ß concentration (pg/ml)
- EP_IN_VITRO_CYTOKINE_RELEASE
  Cytokine concentration (pg/ml)
- EP_CATHEPSINB_RELEASE
  Release concentration pg/ml
- EP_CATHEPSINB_ACTIVITY
  Activity x-fold change over negative control..
- EP_IN_VITRO_GRANULOMA_FORMATION
  Development of 3D granuloma in response to long-term in vitro exposure to NF based on model from Sanchez et al 2011.
  Qualitative Yes/No
- EP_IN_VITRO_GRANULOMA_SIZE
  Mean diameter: µm
  These might just be endpoint parameters of IP_IN_VITRO_GRANULOMA (to be deprecated)

- EP_IN_VITRO_GRANULOMA_TIME
  Days post exposure
  These might just be endpoint parameters of IP_IN_VITRO_GRANULOMA (to be deprecated)
- EP_IN_VIVO_CELL_COUNT
  Absolute: #/L
  Relative: %
- EP_IN_VIVO_NEUTROPHIL_INFLUX
  Absolute: #/L
  Relative: %
- EP_IN_VIVO_MACROPHAGE_COUNT
  Absolute: #/L
  Relative: %
- EP_IN_VIVO_CYTOKINE_RELEASE
  Cytokine conc.: pg/mL
- EP_IN_VIVO_INFLAMMATION
  #/# animals with minimal, slight, moderate, marked or massive bronchiolar/ alveolar inflammation
- EP_LYSOSOMAL_DISRUPTION
  Qualitative Yes|No

HH_FIBROSIS

- EP_FIBROSIS
  Is this an effect endpoint of cytotoxicity or a category on its own?

HH_OXIDATIVE_STRESS

Oxidative stress is caused by the presence of any of a number of reactive oxygen species (ROS) which the cell is unable to counterbalance. The result is damage to one or more biomolecules including DNA, RNA, proteins and lipids. Oxidative stress has been implicated in the natural aging process as well as a variety of disease states:
ENM_0000037

- EP_DCFH_RFU_CHANGE
  Change in RFU (Relative Fluorescent Unit)
- EP_NRF2_LUCIFERASE_ACTIVITY
- EP_NRF2_FOLD_LUCIFERASE_ACTIVITY_INDUCTION
- EP_DCFH_AIR_LIQUID_INTERFACE_PERC_OF_CONTROL
- EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL
- EP_CHANGE_IN_GSH_LEVEL
  CHANGE IN GSH LEVEL
- EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION
- EP_MDA_LIPID_PEROXIDATION
- EP_IN_VITRO_MDA_OXIDATIVE_STRESS_QUANTIFICATION
- EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN
- EP_IN_VITRO_HMOX_OXIDATIVE_STRESS_NFOLD_NEG_CONTROL

HH_CELLULAR_INTERNALIZATION

Introduced by H-O-1a

HH_CARCINOGENICITY

OHT 72: Carcinogenicity

HH_REPRODUCTION

OHT 73: Toxicity to reproduction

HH_DEVELOPMENTAL

OHT 74: Developmental toxicity/teratogenicity

HH_NEUROTOXICITY

OHT 76: Neurotoxicity

HH_IMMUNOTOXICITY

OHT 77: Immunotoxicity
NPO_1339_SECTION

- EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION
  Cytokine concentration (pg/ml)
- EP_HEAT_SHOCK_PROTEIN_PERC_OF_CONTROL

HH_BARRIER_INTEGRITY

Barrier integrity

- EP_INVITRO_BARRIER_INTEGRITY
  NANoREG D5.03 DR, SOP 03 Ohm/cm2
- EP_TEER_DECREASE_VERSUS_CONTROL
- EP_IN_VITRO_INTESTINAL_MICROBIOTA_INTEGRITY

HH_LUNG_DEPOSITION

Newly introduced IATA H-I-1 (perhaps move as HH_LUNG_DEPOSITION?)

- EP_DEPOSITION_FRACTION_TRACHEA_BRONCHI
  deposition
- EP_DEPOSITION_FRACTION_ALVEOLI

UE_MANUFACTURE

OHT 301: Use and exposure information: Manufacture
This stage includes processes by which the registered substance is manufactured from raw materials. Operations which are necessary for the handling of a substance on its own in the manufacturing for export or placing on the EU market are considered to be part of the manufacturing stage (e.g. filling into appropriate containers, storage, addition of stabiliser, dilution to a safer concentration -if necessary for transport safety-). If a substance is directly exported after manufacture, all activities with the substance refer to manufacturing and should be reported under this stage. (Ref: ECHA, Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description. Version 3.0 2015)

UE_FORMULATING_REPACKING

OHT 302: Use and exposure information: Formulating or re-packing
A use in the formulation stage corresponds to specific activities meant to produce a mixture to be put on the market. This means that during formulation, the substance is transferred and mixed with other substances. It corresponds to activities taking place at industrial sites. Mixing activities during end use are not to be reported under this formulation stage. Manufacturers' or importers' own formulation should be reported under this life cycle stage.
Chemical distributors' activities such as repacking (which involves transfer of the substance) are to be covered under the formulation stage even if no mixing is carried out. It should be noted that if there is repacking (which is a use), the distributor becomes a downstream user for REACH (with all corresponding duties). This also applies to importers transferring substances from large containers into smaller containers without mixing.
Note that distribution, assembling of small containers for transport or re-labelling activities without transfer of substance are not to be considered as "uses" and have therefore not to be reported. (Ref: ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description Version 3.0 - December 2015)

UE_USES_AT_INDUSTRIAL_SITES

OHT 303: Use and exposure information: Uses at industrial sites
All end-uses of the substance (as such or in a mixture) carried out at industrial sites should be reported under this life cycle stage.
A use is an end-use when as its result the substance:
- has reacted (therefore it does not exist anymore in its original form), or
- has become part of an article, or
- has completely been released via waste water or exhaust air, and/or it is contained in waste from this use.
If the substance becomes part of an article, the subsequent life cycle stage (the service life) is to be reported as well.
Manufacturers' or importers' own (end)-uses should be reported under this life cycle stage. (Ref: ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description Version 3.0 - December 2015)

UE_WIDESPREAD_USE_WORKERS

OHT 304: Use and exposure information: Widespread use by professional workers
Widespread uses by professional workers correspond to uses carried out in the context of commercial activities and assumed to take place in most towns of a certain size, by multiple actors each at low scale e.g. local garage, small cleaning businesses. They are also considered end-uses. The further fate of the substance corresponds to the fate as described for uses at industrial sites.(Ref: ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description Version 3.0 - December 2015)

UE_CONSUMER_USES

OHT 305: Use and exposure information: Consumer uses
All end-uses of the substance as such or in a mixture carried out by consumers can be reported under this life cycle stage. Uses by consumers are also considered to take place in a widespread manner. (Ref: ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description Version 3.0 - December 2015)

UE_SERVICE_LIFE

OHT 306: Use and exposure information: Service Life
For a given substance incorporated into an article, the service life is considered to be the period of time an article remains in service (or in use).
Articles containing the substance can be used or processed by consumers, by workers at industrial sites and/or by professional workers. This also includes processing of semi-finished articles by workers with the aim of producing finished articles or repair and maintenance work like for example sanding of surfaces.
When substances remain in dried coatings, adhesives or comparable mixtures after application in/on the article, one or more uses at service life stage should be reported. If the substance is incorporated in buildings, constructions and parts of them, they should be reported in the same way as when they are incorporated into articles.
Substances for sole use as an intermediate should never have any service life described, as by definition they are transformed during industrial use into another substance, which will then potentially be subject to registration obligations.
During the production of an article a registered substance may react and the transformation product may become part of the article. The parent substance is not regarded as an intermediate (as the transformation product is part of an article), and thus the lifecycle of the substance does not end at transformation. It is therefore expected that the use description of the parent covers the service life stage, even though the parent itself is not present in the article.
In some cases, it might not be easy to determine whether a substance is used as a substance or mixture as such (in which case the use should be documented under the formulation or repacking, industrial, professional or consumer stages) or whether the substance is an integral part of an article. The ECHA Guidance on requirements for substance in articles(https://echa.europa.eu/support/guidance) provides further clarification on the definition of an "article" and decision criteria. (Ref: ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.12: Use description Version 3.0 - December 2015)

HE_EXPOSURE_ORAL

HE_EXPOSURE_INHAL

- EP_EXPOSURE_CONC_NUMB
  The number based average concentration of particles per volume over a certain period of time.
- EP_EXPOSURE_CONC_MASS
  The mass based average concentration of particles per volume over a certain period of time.

HE_EXPOSURE_DERMAL

DataType

The type of data represented by a data object.

- tNUM_Y
  A single numerical value with unit Y
- tNUM_YT
  A single numerical value with unit Y at time t
- tNUM_X
  A single numerical value with unit X
- tNUM_XT
  A single numerical value with unit X at time t
- tNUM_XY
  A numerical datapoint x,y where x has unitX and y has unitY
- tNUM_XYT
  A numerical datapoint x,y where x has unitX and y has unitY at time t
- tENUM
  One enumerate from a closed domain determined by the endpoint descriptor. Qualitative result
- tENUM_Y
  One enumerate from a closed domain determined by the endpoint descriptor of a certain quantity y.
- tENUM_YT
  One enumerate from a closed domain determined by the endpoint descriptor of a certain quantity y at time t.
- tENUM_X
  One enumerate from a closed domain determined by the endpoint descriptor of a certain quantity x.
- tENUM_XY
  One enumerate with a value y for a certain x (e.g. ECx y=mg/l, x=%)
- tENUM_XYT
  One enumerate with a value y for a certain x (e.g. ECx y=mg/l, x=%) at time t
- tTEXT
  Text based data either open or masked

DataOperator

The type of operator applied to the dataobject.
Data reduction from distributions to scalar descriptors.

- oNONE
- oMEAN_XY
  The arithmic mean of the different values Y for the same X. (e.g. averaging dose response curves of different replicates/ experiments)
- oMEAN
  The arithmic mean of scalar values
- oMODE
  The mode of a set of data values is the X-value that appears most often.
- oMODE_2nd
  The second mode of a set of data values is the X-value that appears most often in second place.
- oMODE_3th
  The third mode of a set of data values is the X-value that appears most often in third place.
- oPEAK
  The peak represent the highest number (Y-value) of appearences of the same X-value.
- oPEAK_2nd
  The second peak represents the second highest number (Y-value) of appearences of the same X-value.
- oPEAK_3th
  The third peak represents the third highest number (Y-value) of appearences of the same X-value.
- oMEDIAN
  The median
- oGEOMEAN
- oAUC
  The area under the curve determined by the dataset
- oSLOPE
  The slope of the line
- oMIN
- oMAX
- oNOEC
  NOEC (no observed effect concentration) is the test substance concentration at which no effect is observed.
- oLOEC
  LOEC (lowest observed effect concentration) is the lowest test substance concentration for which the effect is significantly different from control.
- oLOAEC
- oLOAEL
- oIC10
  IC10
- oIC50
  half maximal inhibitory concentration (IC50)
- oEC50
- oNORM
  Data is normalised

DistrQualifier

- dqNO
- dqPLUS_MIN
- dqSD
- dqRSD_PERC
- dqGEOSD

ControlType

- positive
- negative

TopCategory

- TC_P_CHEM
- TC_ENV_FATE
- TC_TOX
- TC_ECOTOX

ResultSourceType

- sEstimated
  Definition: Not based upon any direct measurement.
  Estimated = a 'guess' based on expert judgement, which in turn is probably based on a rough form of read-across from another similar-ish chemical or on simplistic modelling. An estimate is only be acceptable as a starting point, e.g. at early stages of Safe-by-Design. A worst-case type default value is probably not really an estimate, but one of those can also be used in a precautionary approach.
- sMeasured
  Based upon real measurements

Atom

- H
- He
- Li
- Be
- B
- C
- N
- O
- F
- Ne
- Na
- Mg
- Al
- Si
- P
- S
- Cl
- Ar
- K
- Ca
- Sc
- Ti
- V
- Cr
- Mn
- Fe
- Co
- Ni
- Cu
- Zn
- Ga
- Ge
- As
- Se
- Br
- Kr
- Rb
- Sr
- Y
- Zr
- Nb
- Mo
- Tc
- Ru
- Rh
- Pd
- Ag
- Cd
- 'In'
- Sn
- Sb
- Te
- I
- Xe
- Cs

- Ba
- La
- Ce
- Pr
- Nd
- Pm
- Sm
- Eu
- Gd
- Tb
- Dy
- Ho
- Er
- Tm
- Yb
- Lu
- Hf
- Ta
- W
- Re
- Os
- Ir
- Pt
- Au
- Hg
- Tl
- Pb
- Bi
- Po
- At
- Rn
- Fr
- Ra
- Ac
- Th
- Pa
- U
- Np
- Pu
- Am
- Cm
- Bk
- Cf
- Es
- Fm
- Md
- No
- Lr
- Rf
- Db
- Sg
- Bh
- Hs
- Mt
- Ds
- Rg
- Cn
- Uut
- Fl
- Uup
- Lv
- Uus
- Uuo

ToxCategory
- passive
- active

ObservationScale

The scale at which 'particles' are observed.

- atomic
  Observation at the atomic scale
- mesoscopic
  Observation at the individual (non-aggregated) particle level
- macroscopic
  Observation at the aggregated/agglomerated scale

ParticleSizeLevel

Indicates which part of the overall particle the size data/property is related to.

- slConstituentParticleLevel
  The size data is related to the individual constituent particle either individually present or part of the aggregate/agglomerate.
- slAgglomerateLevel
  The size data is related to the entire assembly structure (agglomerate/aggregate) existing out of 1 or more primary constituent particles.

DoseDescriptor
- ADI
- DNEL
- OEL
- PNEC
- EC_x
- LC_x
- IC_x

TreatmentType

Used to indicate what kind of treatment the measured datapoint is related to. The default treatment is trSample, which indicates that

- trSample
  The measurement is conducted on a sample of the tested substance
- trNC_untreated
  The measurement is conducted without the targeted substance and the results are used as a negative control. (in other words a 0% dose)
- trNC_substance
  The measurement is conducted with a negative control substance other than the targeted substance.
- trNC_NoCells
  An in vitro study is conducted without the use of the targeted cell line and the results are used as a negative control. (not sure if the tested material is applied??)
- trPC_substance
  The measurement is conducted with a positive control substance other than the targeted substance. (often no conc/dose is provided for the positive control, why??)

3.2 Defined classes

Class EP_Owner

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Attributes

name	type	domain	inference	comment
log	: XML nodes			*Internal propery used to log xml based notifications generated during loading or validation process.*

Operators

```
function EP_Owner.CategoryEndpointDomain(): Enumerations
| Enumerations{}

procedure EP_Owner.Initialize()
  SyncEndpoints()

function EP_Owner::BI_Qualifiers():: EPQs
| EPQs{}

function EP_Owner.ValueEndpointDomain(): Enumerates
| Enumerates{}

function EP_Owner.DP_From(epq : EP_Qualifier ): EP_DataObject
  /* */

function EP_Owner.DP_FromProvided(epq : EP_Qualifier ): EP_DataObject
  if epq.edit then
  begin
    result := Datapoint_FromEndpointRecords(endpoints, epq)→If(dp | dp, EditableDP_FromProvided(epq))
  end
  else
  begin
    result := Datapoint_FromEndpointRecords(endpoints, epq);
    if result = nil then
      with Convertors(epq) | convertors then
      begin
        with convertors[1] | convertor do
          with convertor.SourceQualifier(epq) | src_epq then
          begin
            with Datapoint_FromEndpointRecords(endpoints, src_epq) | src_dp then
            begin
              with convertor.Convert_DP(src_epq, src_dp, epq) | dp then
              begin
                result := dp
              end
            end
          end
      end  ;
    if result = nil then
      with Calculators(epq) | calculators then
        with calculators[1] | calculator do
          with calculator.Calculate_DP(self, epq) | dp then
          begin
            result := dp
          end
  end
```

Defined composites

Any instance of `EP_Owner` is composed of

- zero or more `endpoints` of `EP_Record`

Class EP_Record

The record representing an endpoint of a certain endpoint category + result endpoint. It acts as a placeholder for the actual dataobject(s) in it.

Attributes

name	type	domain	inference	comment
category_endpoint	:: any Enumeration		Infer category endpoint	*The first level of endpoint description, is used to organize the actual result endpoints. Most category endpoints correspond with the OECD harmonised templates (OHT)*
result_endpoint	:: any Enumerate		Infer result endpoint	*Used to identify the actual property or effect/result endpoint the dataobject in it belongs to.* *A certain endpoint is uniquely identifiied only in the combination of category + result endpoint.*
medium_descriptor	:: MediumDescriptor		Infer medium descriptor	*The medium the result is relevant for.*
cell_line_descriptor	:: any Enumerate		Infer cell descriptor	*The type of cell line or co-culture (combination of cell line types) the data is related to.*
id	: String			*The id attribute should be assigned a corresponding id for that entry in a data-base. If the id is assigned, the endpoint record is assumed to be read-only.*
valid	: Boolean		Infer valid	

Inference methods

Inference method: 'Infer category endpoint'

C1	rec_owner	nil	ELSE				
C2	ByUser(category_endpoint)	-	False			True	
C3	rec_owner.CategoryEndpointDomain() | domain	-	0	1	ELSE	-	
C4	Current(category_endpoint) in rec_owner.CategoryEndpointDomain()	-	-	-	-	True	False
A1	**Reset**(category_endpoint)		X				X
A2	category_endpoint			domain[1]			
		R1	R2	R3	R4	R5	R6

Inference method: 'Infer result endpoint'

C1	rec_owner	nil	ELSE						
C2	ByUser(result_endpoint)	-	False				True		
C3	category_endpoint	-	nil	ELSE			nil	ELSE	
C4	rec_owner.ValueEndpointDomain() | domain	-	-	0	1	ELSE	-	0	ELSE
C5	Current(result_endpoint) in rec_owner.ValueEndpointDomain()	-	-	-	-	-	-	-	True	False
A1	**Reset**(result_endpoint)		X	X			X			X
A2	result_endpoint				domain[1]					
		R1	R2	R3	R4	R5	R6	R7	R8	R9

Inference method: 'Infer medium descriptor'

C1	ByUser(medium_descriptor)	False		True
C2	rec_owner as Assay | assay	nil	ELSE	-
A1	medium_descriptor		assay.medium_descriptor	
A2	**Reset**(medium_descriptor)	X		
		R1	R2	R3

Inference method: 'Infer cell descriptor'

C1	ByUser(cell_line_descriptor)	False		True
C2	rec_owner as Assay | assay	nil	ELSE	-
A1	cell_line_descriptor		assay.cell_line_descriptor	
A2	**Reset**(cell_line_descriptor)	X		
		R1	R2	R3

Inference method: 'Infer valid'

C1		-
A1	valid	dataobjects→Exists(dp | dp.valid)
		R1

Operators

```
constructor EP_Record.Create(epq : EP_Qualifier )
  with self→New | rec then
  begin
    result := rec;
    if (epq ≠ nil) and (epq.endpoint_descriptor ≠ nil) then
    begin
      rec.result_endpoint ?= epq.endpoint_descriptor;
      rec.category_endpoint ?= rec.result_endpoint→Enumeration;
      rec.medium_descriptor ?= epq.medium_qualifier;
      rec.valid := True
    end
  end

function EP_Record.MatchesQualifier(epq : EP_Qualifier ): Boolean
  if (result_endpoint = epq.endpoint_descriptor) and valid then
  begin
    result := (epq.medium_qualifier = nil) or (medium_descriptor = epq.medium_qualifier);
    if result and (epq.assay_descriptor ≠ nil) then
    begin
      if rec_owner is Assay | assay then
        result := assay.assay_descriptor = epq.assay_descriptor
      else
        result := False
    end
  end
```

Defined composites

Any instance of EP_Record is composed of
- zero or more dataobjects of EP_DataObject

Class EP_Qualifier

This class is used to create qualifiers to be used a selectors for endpoints & dataobject in various functions. After creating an EP_Qualifier object and assigning the relevant selection criteria as constants to the appropriate attributes the established qualifier can be passed as an argument in functions and procedures which select or operate on the endpoints and the dataobjects in them.

Attributes

name	type	domain	inference	comment
title	: String			*A qualifier can be assigned a title / abbreviation what the qualifier is used for. [optional, not used as a selecction criterium]*
endpoint_descriptor	:: any Enumerate			*The endpoint descriptor is the result endpoint [enumerate] of a certain category endpoint [enumeration] which represents the specific targeted result endpoint. [required, primary selection criterium]*
assay_descriptor	:: AssayDescriptor			*The assay descriptor can be provided as an additional selection criterium. [optional]*
medium_qualifier	:: any Enumerate			*The medium qualifier can be provided as an additional selection criterium. [optional]*
cell_qualifier	:: any Enumerate			*The cell qualifier can be provided as an additional selection criterium. [optional] This qualifier can hold a specific type of cell but also a generic cell descriptor or co-culture descriptor.*
v_unit	:: Unit		Infer value unit	*Used to select all datapoints with a value corresponding this unit. [optional]*
v_operator	:: DataOperator			*Used to indicate what type of operation is to be selected or performed on the data. For instance, if the v_operator is set to oMEAN, this is used to first find the an existing mean of the qualified data, and in case this fails, the calculate the mean from raw data if available.* *See DataOperator enumeration for more details.*
per_x	: Quantity			*Used to qualify datapoints related to a specific value for x. For example, selecting response values for a certain dose x. [optional]*
at_t	: Time			*Used to qualify datapoints related to a specific duration/time t. For example, selecting values in time related assays, like dissolution or biodegradition at a certain point in time. [optional]*
enum	:: any Enumerate			*Used to qualify datapoints related to a specific enumerate. For example, selecting size values of the [agglomerated level] instead of the [particle constituent level]. [optional]*
edit	: Boolean			*For internal usage, allows selection of incomplete dataobjects to be edited. [optional]*
section	:: Section			*Used to indicate that the qualifier is related to What they do, Where they go etc.. not used for selection as such [optional]*
source_type	:: ResultSourceType			*Used to select dataobjects coming from a specific source like only [measured]. [optional]*

Inference methods

Inference method: 'Infer value unit'

C1	ByUser(v_unit)	True			False			
C2	EP_Units_Y(endpoint_descriptor) | unit_domain	0	ELSE		0	1	ELSE	
C3	unit_domain→Exists(domain_unit | v_unit as domain_unit)	-	True	False	-	-	-	
C4	unit_domain→ForAll(domain_unit | unit_domain[1] as domain_unit)	-	-	-	-	-	True	False
A1	v_unit					unit_domain[1]	unit_domain[1]	
A2	**Reset**(v_**unit**)	X		X	X			X
		R1	R2	R3	R4	R5	R6	R7

Class `EP_DataObject`

Represents a single data entry row of an endpoint record. It can hold a quantitative result as a single value [y] or as a datapoint [x,y], these can also be time based [y,t] or [x,y,t]. It can also hold a qualitative result [enum]. Qualitative and quantitative values are also combined. In case the data is a study result, references to the studied material, the replicate id and experiment nr can be provided. The dataobject is used to allow the user to provide the data for a certain endpoints and also to load a study result row from eNanomapper.

Attributes

name	type	domain	inference	comment
endpoint_qualifier	: EP_Qualifier			*The epq used to qualify this object in case of derived or converted data objects.*
id	: String			*id => the corresponding id in the source database*
data_type	:: DataType		Infer data type	*Indicates which kind of value the data object contains. The qualifier y determines which data fields or combinaitions [value_y, text_y, enum_y, value_x] contain data.*
data_operator	:: DataOperator			*Indicates which kind of operation has been applied relative to the source datapoints. For instance opMEAN indicates that the data represents the mean value of the source data.*
value_y	: Quantity	ep_rec→If(r | CheckValue_Y(self, #), True)		*The y value is the actual response / measured value*
distr_type_y	:: DistrQualifier			*The distribution type indicates which type of distribution value [distr_y]is used for the value_y*
distr_y	: Quantity			*The distr_y value contains the paramater used to express the distribution related to the distr_qualifier_y.*
enum_y	:: any Enumerate	ep_rec→If(r | CheckEnum_Y(self, #), True)		*The enum datafield, in case the qualifier_y = [qENUM, qENUM_VALUE]. In case the qualifier_y = qENUM_VALUE the enum is combined with a quantity in value_y.*
text_y	: String	CheckText_InDomain(self, #)		*The text datafield, in case of qualitative free results.*
value_x	: Quantity	ep_rec→If(r | CheckValue_X(self, #), True)		*The x value is used when the qualifier_y=[qVALUE_X, qMEAN_X, qMEDIAN_X], the x value is used to describe a data value_y for a certain value of x. Think of individual datapoints in a dose response curve, or the percentile in a size distribution.*
time_t	: Time			
material	: String			*Field introduced in eNanomapper, used to indicate if the study result row is a measurement with a sample of the studied material, or another material like a positive control or benchmark material etc..* *Needs to be revised as it is currently open text and used in different ways.*
replicate	: String			*Used to identify which data objects belong to the same replicate.*
experiment	: String			
source_type	:: ResultSourceType		Infer source type	*Used to indicate whether the data is based on estimations or measurement.*
valid	: Boolean		Infer valid	*Indicates if the data object is complete and relevant data fields known and within all contraints. Only valid data objects are used during the assessment.*
log	: XML nodes			*Used to log errors, remarks for instance during the import of data from an external database.*

Inference methods

Inference method: 'Infer valid'

C1	source_dps	0																			ELSE
C2	ep_rec	nil	ELSE																		–
C3	ep_rec.result_endpoint	–	nil	ELSE																	–
C4	data_type	–	–	tNUM_Y		tNUM_XY			tENUM		tENUM_Y			tENUM_XY				tTEXT		ELSE	–
C5	Known(value_x) and CheckValue_X(self, Current(value_x))	–	–	–		True		False	–		–			True			False	–		–	–
C6	Known(value_y) and CheckValue_Y(self, Current(value_y))	–	–	True	False	True	False	–	–		True		False	True		False		–		–	–
C7	Known(enum_y) and CheckEnum_Y(self, Current(enum_y))	–	–	–	–	–	–	–	True	False	True	False	–	True	False	–	–	–		–	–
C8	Known(text_y) and CheckText_InDomain(self, Current(text_y))	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	True	False	–	–
A1	valid	False	False	True	False	True	False	False	True	False	True	False	False	True	False	False	False	True	False		
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20

Inference method: 'Infer data type'

C1	ep_rec	nil	ELSE				
C2	ByUser(data_type)	–	False		True		
C3	EP_DataType(ep_rec.result_endpoint, data_operator) | dt	–	nil	ELSE	nil	ELSE	
C4	Current(data_type) = dt	–	–	–	–	True	False
A1	data_type			dt			
A2	**Reset**(data_**type**)	X	X		X		X
		R1	R2	R3	R4	R5	R6

Inference method: 'Infer source type'

C1	ByUser(source_type)	False					True
C2	ep_rec	nil	ELSE				–
C3	ep_rec as Assay | assay	–	nil			ELSE	–
C4	ep_rec.rec_owner	–	nil		ELSE	–	–
C5	source_dps→ForAll(sdp | sdp.source_type = sMeasured)	–	True	False	–	–	–
A1	source_type	sEstimated	sMeasured	sEstimated	sEstimated	sMeasured	
		R1	R2	R3	R4	R5	R6

Class **EndpointsConstraint**

Used to define constraining relationships between different endpoints of the same material or assay

Defined expressions

name	type	expression	comment
ep1	:: any Enumerate	**nil**	
ep2	:: any Enumerate	**nil**	

Operators

```
function EndpointsConstraint::WithinConstrains( this_dp : EP_DataObject, other_dps : EP_Datapoints, v : Unit ):: Boolean
  begin
    result := True;
    with this_dp.ep_rec | ep then
    begin
      if (ep.result_endpoint = ep1) or (ep.result_endpoint = ep2) then
      begin
        /* This endpoint is related */      ;
        /* Only data of endpoints belonging to the same owner (material, assay) may have constrains*/      ;
        with (ep.result_endpoint = ep1)→If(ep2, ep1) | other_ep do
        begin
          /* Only data of the correct constraining endpoint and same replicate and same experiment */        ;
          with other_dps→Select(mdp | Current(mdp.valid) and (mdp.ep_rec.result_endpoint = other_ep) and (mdp.replicate = this_dp.replicate) and (mdp.experiment = this_dp.experiment) and (mdp.material = this_
            dp.material)) | relevant_dps then
          begin
            result := relevant_dps→ForAll(rdp | WithinConstrainsDecision(this_dp, rdp, v))
          end
        end
      end
    end
  end

function EndpointsConstraint::WithinConstrainsDecision( this_dp : EP_DataObject, other_dp : EP_DataObject, v : Unit ):: Boolean
|  True
```

Class **Dn1_Dn3_SizeConstraint** is kind of **EndpointsConstraint**

Used to define constraining relationships between different endpoints of the same material or assay

Defined expressions

name	type	expression	comment
ep1	: any Enumerate	EP_DnPx_D1	
ep2	: any Enumerate	EP_DnPx_D3	

Operators

function Dn1_Dn3_SizeConstraint.WithinConstrainsDecision(this_dp : EP_DataObject, other_dp : EP_DataObject, v : Unit): Boolean [specialization]

C1	Known(other_dp.value_y)	True						False
C2	v is Length	True					False	-
C3	other_dp.value_y is Length	True				False	-	-
C4	this_dp.enum_y = other_dp.enum_y	True			False	-	-	-
C5	this_dp.value_x = other_dp.value_x	True		False	-	-	-	-
C6	this_dp.ep_rec.result_endpoint	EP_DnPx_D1	EP_DnPx_D3	-	-	-	-	-
A1	result	v ≤ other_dp.value_y	v ≥ other_dp.value_y	True	True	True	True	True
		R1	R2	R3	R4	R5	R6	R7

Class **EndpointConvertor**

Used to convert one endpoint into another one.

Defined expressions

name	type	expression	comment
conv_eps	: Enumerates	Enumerates{}	

Operators

```
function EndpointConvertor::SourceQualifier(dest_epq : EP_Qualifier ):: EP_Qualifier
| nil

function EndpointConvertor::Convert_DP(src_epq : EP_Qualifier,src_dp : EP_DataObject,dest_epq : EP_Qualifier ):: EP_DataObject
| nil

function EndpointConvertor::MatchConversionEndpoint(dest_epq : EP_Qualifier ):: Boolean
| dest_epq→If(epq | epq.endpoint_descriptor in conv_eps, False)

function EndpointConvertor::Convert_EP(src_epq : EP_Qualifier,src_dp : EP_DataObject,dest_epq : EP_Qualifier ):: EP_Record
  with Convert_DP(src_epq, src_dp, dest_epq) | dp then
  begin
    result := EP_Record.Create(dest_epq);
    result→AddComponent(dataobjects, dp)
  end
```

Class `AspectRatio_Convertor` is kind of `EndpointConvertor`

Converts AR minor/major into major/minor visa versa.

Defined expressions

name	type	expression	comment
conv_eps	: Enumerates	Enumerates{PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1, PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3}	

Operators

function AspectRatio_Convertor.SourceQualifier(dest_epq : EP_Qualifier): EP_Qualifier [specialization]

C1	dest_epq	nil	ELSE		
C2	dest_epq.endpoint_descriptor	-	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3	ELSE
A1	result := ENUM(EPQ(#), dest_epq.enum)		PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1	
		R1	R2	R3	R4

function AspectRatio_Convertor.Convert_DP(src_epq : EP_Qualifier, src_dp : EP_DataObject, dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	src_epq.endpoint_descriptor	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1			PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3			ELSE
C2	dest_epq.endpoint_descriptor	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3		ELSE	PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1		ELSE	-
C3	Known(src_dp.value_y)	True	False	-	True	False	-	-

A1	with EP_DataObject→New | dp then
	begin
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := src_dp;
	  dp.enum_y := src_epq.enum;
	  dp.value_y := 1 / src_dp.value_y;
	  dp.valid := True
	end
		X			X			

		R1	R2	R3	R4	R5	R6	R7

Class SpacegroupToCrystalSystem is kind of EndpointConvertor

Converts a spacegroup (number) into the corresponding crystal system.

Defined expressions

name	type	expression	comment
conv_eps	: Enumerates	Enumerates{PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM}	

Operators

function SpacegroupToCrystalSystem.SourceQualifier(dest_epq : EP_Qualifier): EP_Qualifier [specialization]

C1	dest_epq	nil	ELSE	
C2	dest_epq.endpoint_descriptor	-	PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM	ELSE
A1	result := EPQ(PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP)		X	
		R1	R2	R3

function SpacegroupToCrystalSystem.Convert_DP(src_epq : EP_Qualifier, src_dp : EP_DataObject, dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	src_epq.endpoint_descriptor	PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP									ELSE
C2	dest_epq.endpoint_descriptor	PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM								ELSE	-
C3	src_dp.enum_y ≠ nil	True							False	-	-
C4	src_dp.enum_y→IndexOf | spg	spg ≤ 2	spg ≤ 15	spg ≤ 74	spg ≤ 142	spg ≤ 167	spg ≤ 194	spg ≤ 230	ELSE	-	-	-
A1	with EP_DataObject→New | dp then begin result := dp; dp.endpoint_qualifier ?= dest_epq; dp.source_dps := src_dp; dp.enum_y := #; dp.valid := True end	'triclinic'	'monoclinic'	'orthorhombic'	'tetragonal'	'trigonal'	'hexagonal'	'cubic'	'amorphous'			
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11

Class Feret_D1_To_DnPx_D1 is kind of EndpointConvertor

Converts a Feret D1 diameter (median) into Dn50 size

Defined expressions

name	type	expression	comment
conv_eps	: Enumerates	Enumerates{PC_GRANULOMETRY::EP_DnPx_D1}	

Operators

function Feret_D1_To_DnPx_D1.SourceQualifier(dest_epq : EP_Qualifier): EP_Qualifier [specialization]

C1	dest_epq	nil	ELSE		
C2	dest_epq.endpoint_descriptor	-	PC_GRANULOMETRY::EP_DnPx_D1		ELSE
C3	dest_epq.per_x as ·% | perc	-	50.0·%	ELSE	-
A1	result := OP(ENUM(EPQ(PC_GRANULOMETRY::EP_FERET_DIAMETER_D1), dest_epq.enum), oMEDIAN)		X		
		R1	R2	R3	R4

function Feret_D1_To_DnPx_D1.Convert_DP(src_epq : EP_Qualifier, src_dp : EP_DataObject, dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	src_epq.endpoint_descriptor	PC_GRANULOMETRY::EP_FERET_DIAMETER_D1		ELSE
C2	src_epq.v_operator	oMEDIAN	ELSE	-

A1	**with** EP_DataObject→**New** | dp **then**
	begin
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := src_dp;
	  dp.value_y := src_dp.value_y;
	  dp.value_x := 50.0·%;
	  dp.enum_y := src_epq.enum;
	  dp.valid := True
	end
		X		

		R1	R2	R3

Class `Feret_D3_To_DnPx_D3` is kind of `EndpointConvertor`

Used to convert one endpoint into another one.

Defined expressions

name	type	expression	comment
conv_eps	: Enumerates	Enumerates{PC_GRANULOMETRY::EP_DnPx_D3}	

Operators

function Feret_D3_To_DnPx_D3.SourceQualifier(dest_epq : EP_Qualifier): EP_Qualifier [specialization]

C1	dest_epq	nil	ELSE		
C2	dest_epq.endpoint_descriptor	-	PC_GRANULOMETRY::EP_DnPx_D3		ELSE
C3	dest_epq.per_x as ·% | perc	-	50.0·%	ELSE	-
A1	result := OP(ENUM(EPQ(PC_GRANULOMETRY::EP_FERET_DIAMETER_D3), dest_epq.enum), oMEDIAN)		X		
		R1	R2	R3	R4

function Feret_D3_To_DnPx_D3.Convert_DP(src_epq : EP_Qualifier , src_dp : EP_DataObject , dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	src_epq.endpoint_descriptor	PC_GRANULOMETRY::EP_FERET_DIAMETER_D3		ELSE
C2	src_epq.v_operator	oMEDIAN	ELSE	-

A1	**with** EP_DataObject→**New** | dp **then**
	begin
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := src_dp;
	  dp.value_y := src_dp.value_y;
	  dp.value_x := 50.0·%;
	  dp.enum_y := src_epq.enum;
	  dp.valid := True
	end
		X		

		R1	R2	R3

Class **EndpointCalculator**

Used to calculate/estimate an endpoint based other available endpoints.

Operators

function EndpointCalculator::MatchCalculationEndpoint(epq : EP_Qualifier):: Boolean
| False

function EndpointCalculator::Calculate_DP(ep_context : EP_Owner , dest_epq : EP_Qualifier):: EP_DataObject
/* TO BE OVERRIDDEN PER CALCULATOR */

function EndpointCalculator::Calculate_EP(ep_context : EP_Owner , dest_epq : EP_Qualifier):: EP_Record
with Calculate_DP(ep_context, dest_epq) | dp **then**
begin
result := EP_**Record**.Create(dest_epq);
result→AddComponent(dataobjects, dp)
end

Class **AerodynamicDiameterCalc** is kind of **EndpointCalculator**

Used to calculate/estimate an endpoint based other available endpoints.

Operators

function AerodynamicDiameterCalc.MatchCalculationEndpoint(epq : EP_Qualifier): Boolean [specialization]
| epq.endpoint_descriptor = PC_GRANULOMETRY::EP_AERODYNAMIC_EQ_SPHERE_DIAMETER

function AerodynamicDiameterCalc.Calculate_DP(ep_context : EP_Owner , dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	ep_context	nil	ELSE		
C2	ep_context.DP_From(EPQU(PC_DENSITY::EP_SKELETAL_DENSITY, ·g·cm⁻³)) | skeletal_density_dp	-	nil	ELSE	
C3	ep_context.DP_From(PER(EPQU(PC_GRANULOMETRY::EP_DnPx_D1, ·nm), 50.0·%)) | Dn50_size_dp	-	-	nil	ELSE

A1	**with** EP_DataObject→**New** | dp **then**
	begin
	  /* Recommended in IATA H-I-2 */ ;
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := EP_Datapoints{skeletal_density_dp, Dn50_size_dp};
	  dp.value_y := Dn50_size_dp.value_y * ((skeletal_density_dp.value_y / 1.0·g·cm⁻³) ^ 0.5);
	  dp.valid := True
	end
					X

		R1	R2	R3	R4

Class **EquivalentVolumeDiameterCalc** is kind of **EndpointCalculator**

[PC_GRANULOMETRY:: EP_VOLUME_EQ_SPHERE_DIAMETER]
*Elongated => (1.5 * particle_diameter^3 * aspect_ratio)→Sqr(3) Sturm 2009 doi:10.1016/j.jhazmat.2009.04.107*
*Platelets => (1.5 * (thickness / diameter)→Sqr(3))*diameter https://www.tandfonline.com/doi/pdf/10.1080/02786828808959176*
TO DO Needs further development also taken shape into account.

Operators

function EquivalentVolumeDiameterCalc.MatchCalculationEndpoint(epq : EP_Qualifier): Boolean [specialization]
| epq.endpoint_descriptor = PC_GRANULOMETRY::EP_VOLUME_EQ_SPHERE_DIAMETER

function EquivalentVolumeDiameterCalc.Calculate_DP(ep_context : EP_Owner , dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	ep_context.DP_From(PER(EPQU(PC_GRANULOMETRY::EP_DnPx_D1, ·nm), 50.0·%)) | dp_particle_size	nil	ELSE	
C2	ep_context.DP_From(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1)) | dp_aspect_ratio	-	nil	ELSE

A1	**with** EP_DataObject→**New** | dp **then**
	begin
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := EP_Datapoints{dp_particle_size, dp_aspect_ratio};
	  dp.value_y := ((1.5 * dp_particle_size.value_y ^ 3) * dp_aspect_ratio.value_y) ^ (1 / 3);
	  dp.valid := True
	end
				X

		R1	R2	R3

Class **DissolutionHalftimeCalc** is kind of **EndpointCalculator**

Used to calculate/estimate an endpoint based other available endpoints.

Operators

function DissolutionHalftimeCalc.MatchCalculationEndpoint(epq : EP_Qualifier): Boolean [specialization]
| epq.endpoint_descriptor = PC_WATER_SOL::EP_DISSOLUTION_HALF_**TIME**

function DissolutionHalftimeCalc.Calculate_DP(ep_context : EP_Owner, dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	dest_epq.medium_qualifier | medium	nil	ELSE				
C2	ep_context.DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_RATE, ·ng·cm⁻²·h⁻¹), medium)) | dp_rate	-	nil	ELSE			
C3	ep_context.DP_From(EPQU(PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA, ·m²·g⁻¹)) | dp_mssa	-	-	nil	ELSE		
C4	dp_mssa.value_y * dp_rate.value_y | freq	-	-	-	freq > 0.0·h⁻¹	ELSE	

A1	**with** EP_DataObject→**New** | dp **then**
	begin
	  result := dp;
	  dp.endpoint_qualifier ?= dest_epq;
	  dp.source_dps := EP_Datapoints{dp_rate, dp_mssa};
	  dp.value_y := (2→**Ln**) / freq;
	  dp.valid := True
	end
					X		

		R1	R2	R3	R4	R5	

Class **sBOD_Calc** is kind of **EndpointCalculator**

Used to calculate/estimate an endpoint based other available endpoints.

Operators

function sBOD_Calc.MatchCalculationEndpoint(epq : EP_Qualifier): Boolean [specialization]
| epq.endpoint_descriptor = EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE

function sBOD_Calc.Calculate_DP(ep_context : EP_Owner, dest_epq : EP_Qualifier): EP_DataObject [specialization]

C1	ep_context.DP_From(MED(EPQU(PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_PER_DOSE, ·m²·l⁻¹), medium)) | ep_BOD_s	nil	ELSE
C2		-	-
A1			
		R1	R2

Class **RelevanceObj**

Used to hold the relevant value ranges for a certain endpoint.

Attributes

name	type	domain	inference	comment
measurable_min	: Quantity			*the lowest measurable value for an endpoint*
measurable_max	: Quantity			*the highest measurable value for an endpoint*
bio_relevance_min	: Quantity			*the lowest biological relevant value for an endpoint*
bio_relevance_max	: Quantity			*the highest biological relevant value for an endpoint*
match_threshold	: Real			*a score equal or below this threshold is considered similar enough to be a direct match*
nomatch_threshold	: Real			*a similarity score above this threshold is considered a mismatch between the two objects for this endpoint*

3.3 Defined associations

Association **datapoint_derivation**

- zero or more source_dps of EP_DataObject
- zero or more derived_dps of EP_DataObject

3.4 Defined collections

EP_RecordClasses defines a sequence containing EP_Record types.
EPQs defines a sequence containing EP_Qualifier objects.
EP_Records defines a sequence containing EP_Record objects.
EP_Datapoints defines a sequence containing EP_DataObject objects.
DataTypes defines a sequence containing DataType enumerates.
ConstraintClasses defines a sequence containing any kind of EndpointsConstraint types.
ConvertorClasses defines a sequence containing any kind of EndpointConvertor types.
CalculatorClasses defines a sequence containing any kind of EndpointCalculator types.
DataOperators defines a sequence containing DataOperator enumerates.
DistributionTypes defines a sequence containing DistrQualifier enumerates.

Operators

```
function ENDPOINT_KB::EP_Units_Y(ep_descriptor :: any Enumerate ):: Units
  case ep_descriptor of
    PC_CLASSIFICATION_LABELING::CLP_HCODE_GENERIC_CONC_LIMIT, PC_CLASSIFICATION_LABELING::CLP_HCODE_SPECIFIC_CONC_LIMIT:
      result := Units{·%};
    PC_CLASSIFICATION_LABELING::CLP_HCODE_M_FACTOR:
      result := Units{Real};
    PC_COMPOSITION::EP_MASS_CONC, PC_COMPOSITION::EP_PURITY:
      result := Units{·%};
    PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC:
      result := Units{·%, ·mg·kg⁻¹};
    PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC:
      result := Units{·%};
    PC_MELTING::EP_MELTING_POINT, PC_BOILING::EP_BOILING_POINT:
      result := Units{·K, ·°C, ·°F};
    PC_CRYSTALLINE_PHASE::EP_CRYSTALLINITY, PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM, PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP, PC_ASPECT_RATIO_SHAPE::EP_SHAPE_CATEGORY:
      result := Units{·%};
    PC_RIGIDITY::EP_YOUNGS_MODULUS, PC_RIGIDITY::EP_SHEAR_MODULUS:
      result := Units{·GPa};
    PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS, PC_DUSTINESS::EP_THORACIC_DUST_INDEX_MASS, PC_DUSTINESS::EP_INHALABLE_DUST_INDEX_MASS:
      result := Units{·mg·kg⁻¹};
    PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_NUMB, PC_DUSTINESS::EP_THORACIC_DUST_INDEX_NUMB, PC_DUSTINESS::EP_INHALABLE_DUST_INDEX_NUMB:
      result := Units{·mg⁻¹};
    PC_AEROSOL_CHARACTERISATION::EP_AEROSOLISED_PARTICLE_CONC:
      result := Units{·cm⁻³};
    PC_GRANULOMETRY::EP_NOMINAL_DIAMETER, PC_GRANULOMETRY::EP_NOMINAL_LENGTH, EP_CONSTITUENT_PARTICLE_SIZE, EP_FERET_DIAMETER_D1, EP_FERET_DIAMETER_D3, EP_LARGEST_INTERNAL_CIRCLE, EP_LEGENDRE_ELLIPSE_D1, EP_SURFACE_
      EQ_SPHERE_DIAMETER, EP_GEOMETRIC_MEAN_DIAMETER, EP_SIEVE_EQ_SPHERE_DIAMETER, EP_ELECTRICAL_MOBILITY_EQ_SPHERE_DIAMETER, EP_STOKES_EQ_SPHERE_DIAMETER, EP_VOLUME_EQ_CYLINDER_LENGTH, EP_VOLUME_EQ_CYLINDER_
      DIAMETER, EP_VOLUME_EQ_DISC_THICKNESS, EP_LEGENDRE_ELLIPSE_D3, EP_VOLUME_EQ_DISC_DIAMETER, EP_VOLUME_EQ_SPHERE_DIAMETER, EP_GEODESIC_THICKNESS, EP_DnPx_D1, EP_DnPx_D2, EP_DnPx_D3, EP_DmPx_D1, EP_DmPx_D2, EP_
      DmPx_D3, EP_DvPx_D1, EP_DvPx_D2, EP_DvPx_D3, EP_DsPx_D1, EP_DsPx_D2, EP_DsPx_D3, EP_DiPx_D1, EP_DiPx_D2, EP_DiPx_D3, EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER, PC_GRANULOMETRY::EP_GEODESIC_LENGTH_D3, EP_PRIMARY_
      PARTICLE_DIAMETER, EP_PRIMARY_PARTICLE_LENGTH:
      result := Units{·nm, ·µm};
    PC_CRYSTALLITE_AND_GRAIN_SIZE::EP_CRYSTALLITE_SIZE, PC_CRYSTALLITE_AND_GRAIN_SIZE::EP_GRAIN_SIZE:
      result := Units{·nm};
    EP_Z_AVERAGE_DIAMETER, EP_INTENSITY_WEIGHTED_SIZE, EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER, EP_EQUIVALENT_CIRCLE_DIAMETER, EP_AERODYNAMIC_EQ_SPHERE_DIAMETER, EP_STATIC_BENDING_PERSISTENCE_LENGTH, EP_CONTOUR_LENGTH, EP_
      RADIUS_OF_GYRATION:
      result := Units{·nm, ·µm};
    EP_FULL_WIDTH_AT_HALF_MAXIMUM:
      result := Units{·nm};
    PC_GRANULOMETRY::EP_RELATIVE_INTENSITY:
      result := Units{Real, ·%};
    EP_ASPECT_RATIO_D3_D1, EP_ASPECT_RATIO_D1_D3, EP_ELLIPSE_RATIO_D3_D1, EP_ELLIPSE_RATIO_D1_D3, EP_CIRCULARITY, EP_ROUNDNESS, EP_COMPACTNESS, EP_CIRCULARITY_FORM_FACTOR, EP_SOLIDITY, EP_CONVEXITY, EP_DYNAMIC_SHAPE_
      FACTOR, EP_MODE_COUNT, EP_DISPERSITY, EP_DISPERSITY_2, EP_AA_INDEX, EP_AA_RATIO, EP_FRACTAL_DIMENSION, EP_SURFACE_AREA_TO_VOLUME_RATIO:
      result := Units{Real};
    EP_SURFACE_AREA:
      result := Units{·m²};
    EP_MASS_SPECIFIC_SURFACE_AREA, EP_SBET, EP_MASS_MICROPOROSITY_SURFACE, EP_MASS_EXTERNAL_SURFACE:
      result := Units{·m²·g⁻¹};
    EP_VOLUME_SPECIFIC_SURFACE_AREA, EP_VOLUME_EXTERNAL_SURFACE:
      result := Units{·m²·cm⁻³};
    EP_TRUE_DENSITY, EP_ABSOLUTE_POWDER_DENSITY, EP_APPARENT_PARTICLE_DENSITY, EP_APPARENT_POWDER_DENSITY, EP_BULK_DENSITY, EP_EFFECTIVE_DENSITY, EP_ENVELOPE_DENSITY, EP_SKELETAL_DENSITY, EP_TAP_DENSITY, EP_
      THEORETICAL_DENSITY:
      result := Units{·g·cm⁻³};
    EP_RELATIVE_DENSITY:
      result := Units{Real, ·%};
    EP_TITRATOR_VOLUME:
      result := Units{·ml};
    PC_POROSITY::EP_PORE_RADIUS:
      result := Units{·nm};
    EP_SPECIFIC_PORE_VOLUME:
      result := Units{·cm³·g⁻¹};
    EP_OXIDATIVE_DAMAGE_PER_DOSE:
      result := Units{·nmol·l⁻¹};
    EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE:
      result := Units{·nmol·mg⁻¹};
    EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE:
      result := Units{·nmol·m⁻²};
    PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_SCORE_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_SPIN_COUNT_PER_SURFACE_CONC, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_
      MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_FRAS_SCORE_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_FRAS_SCORE_SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_MASS, PC_RADICAL_FORMATION_
      POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_SURF:
      result := Units{Real};
    PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_OXIDATION_MASS:
      result := Units{·%};
    PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU, EP_DCFH_ROS_GENERATION_AU, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY:
      result := Units{·AU};
    PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL, EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_ALAMAR_BLUE_
      CYTOTOXICITY_PERC_OF_CONTROL, EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL, EP_NRU_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_RESAZURIN_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_IAAC_CYTOTOXICITY_PERC_OF_
      CONTROL, HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_CFE_CYTOTOXICITY_PERC_OF_CONTROL:
      result := Units{·%};
    PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_SURFACE, EP_DCFH_INTRINSIC_ROS_CHANGE_IN_RFU:
      result := Units{Real};
```

```
PC_BIOMOL_INTERACTION::EP_BINDING_ENERGY, PC_BIOMOL_INTERACTION::EP_BINDING_ENTHALPY:
  result := Units{·kJ·mol⁻¹};
PC_BIOMOL_INTERACTION::EP_BINDING_ENTROPY:
  result := Units{·J·mol⁻¹·K⁻¹};
HH_OXIDATIVE_STRESS::EP_DCFH_AIR_LIQUID_INTERFACE_PERC_OF_CONTROL, HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL, HH_OXIDATIVE_STRESS::EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN:
  result := Units{·%};
HH_OXIDATIVE_STRESS::EP_DCFH_RFU_CHANGE:
  result := Units{Real};
HH_IMMUNOTOXICITY::EP_HEAT_SHOCK_PROTEIN_PERC_OF_CONTROL:
  result := Units{·%};
EP_PERCENTAGE_DISSOLVED:
  result := Units{·%};
EP_DISSOLUTION_MASS_LOSS:
  result := Units{·%·h⁻¹};
EP_DISSOLUTION_RATE:
  result := Units{·ng·cm⁻²·h⁻¹};
EP_DISSOLUTION_HALF_TIME, EP_RETAINED_FIBRE_HALF_TIME, EP_INTRACELLULAR_DISSOLUTION_HALF_TIME:
  result := Units{·min, ·h, ·d};
EP_ZETA_POTENTIAL:
  result := Units{·mV};
PC_NON_SATURATED_PH::EP_PH, EP_ISOELECTRIC_POINT:
  result := Units{Real};
PC_STABILITY_THERMAL_SUNLIGHT_METALS::EP_MASS_LOSS, PC_STABILITY_THERMAL_SUNLIGHT_METALS::EP_MASS_LOSS_WATER, EP_INTRACELLULAR_DISSOLUTION_RATE:
  result := Units{·%};
EP_DNA_STRAND_BREAKS, EP_FPG_SENSITIVE_SITES:
  result := Units{·%};
EP_DISPERSION_STABILITY:
  result := Units{·%};
EP_DEPOSITION_FRACTION_TRACHEA_BRONCHI, EP_DEPOSITION_FRACTION_ALVEOLI:
  result := Units{·%};
PC_SURFACE_TENSION::EP_WATER_CONTACT_ANGLE, PC_HYDROPHOBICITY::EP_WATER_CONTACT_ANGLE:
  result := Units{·°};
PC_WATER_SOL::EP_SOLUBILITY:
  result := Units{·ppm};
PC_WATER_SOL::EP_WATER_SOL:
  result := Units{·µg·l⁻¹, ·g·l⁻¹};
EP_RETAINED_FIBRE_BURDEN:
  result := Units{·mg·g⁻¹};
EP_TRANSFORMATION_D1, EP_TRANSFORMATION_D3, EP_TRANSFORMATION_MORPHOLOGY:
  result := Units{·%};
EC_ALGAE_TOX::EP_GROWTH, EC_ALGAE_TOX::EP_YIELD, EC_ALGAE_TOX::EP_BIOMASS:
  result := Units{·mg·l⁻¹};
EC_BAC_TOX::EP_GROWTH_INHIBITION, EC_BAC_TOX::EP_NITRIFICATION_INHIBITION, EP_RESPIRATION_INHIBITION:
  result := Units{·%};
EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION, EC_SEDIMENT_TOX::EP_SURVIVAL:
  result := Units{·mg·l⁻¹, ·mg·kg⁻¹};
EC_FISH_TOX_SHORT::EP_LYSOSOMAL_INTEGRITY, EC_FISH_TOX_SHORT::EP_METABOLIC_ACTIVITY, EC_FISH_TOX_SHORT::EP_PLASMA_MEMBRANE_INTEGRITY, EC_FISH_TOX_SHORT::EP_MORTALITY, EC_FISH_TOX_SHORT::EP_DEVELOPMENT:
  result := Units{·µg·ml⁻¹, ·mg·l⁻¹};
EC_FISH_TOX_CHRONIC::EP_SURVIVAL, EC_FISH_TOX_CHRONIC::EP_WEIGHT, EC_FISH_TOX_CHRONIC::EP_LENGTH, EC_FISH_TOX_CHRONIC::EP_ABNORMAL_APPEARANCE_AND_BEHAVIOR, EC_FISH_TOX_CHRONIC::EP_HATCHING, EC_FISH_TOX_
  CHRONIC::EP_GROWTH:
  result := Units{·mg·l⁻¹};
EC_AQUATIC_INVERT_TOX_CHRONIC::EP_IMMOBILIZATION:
  result := Units{·mg·l⁻¹};
EC_AQUATIC_INVERT_TOX_SHORT::EP_MORTALITY, EC_AQUATIC_INVERT_TOX_SHORT::EP_GROWTH, EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION:
  result := Units{·mg·l⁻¹};
EC_AQ_PLANTS_NONE_ALGAE::EP_GROWTH, EC_AQ_PLANTS_NONE_ALGAE::EP_YIELD:
  result := Units{·mg·l⁻¹};
EP_DERIVED_COUNT_RATE:
  begin
    /* The actual unit of the count rate is Kcps = Kilo counts per second  1000 photons per second  */      ;
    result := Units{·k1·s⁻¹}
  end;
EP_VAPOUR_PRESSURE:
  result := Units{·Pa};
EP_LOG_POW:
  result := Units{Real};
EP_VISCOSITY:
  result := Units{·m²·s⁻¹};
EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG:
  result := Units{·%};
HH_BASIC_TOX::EP_IN_VIVO_ACCUMULATION:
  result := Units{·mg·kg⁻¹};
HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE, HH_INFLAMMATION::EP_CATHEPSINB_RELEASE:
  result := Units{·pg·ml⁻¹, ·µg·ml⁻¹};
HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE, HH_CYTOTOXICITY::EP_NORMALISED_POST_EXPOSURE_CELL_INDEX_1:
  result := Units{·%};
HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx:
```

```
    result := Units{·mg·g^-1};
  HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_TIME:
    result := Units{·d};
  HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE:
    result := Units{·µg·d^-1};
  HH_OXIDATIVE_STRESS::EP_NRF2_LUCIFERASE_ACTIVITY, EP_NRF2_FOLD_LUCIFERASE_ACTIVITY_INDUCTION, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_450_NM, HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM, HH_
     OXIDATIVE_STRESS::EP_CHANGE_IN_GSH_LEVEL:
    result := Units{Real};
  HH_OXIDATIVE_STRESS::EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION:
    result := Units{·µM};
  HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_NM:
    result := Units{·OD};
  HH_OXIDATIVE_STRESS::EP_MDA_LIPID_PEROXIDATION:
    result := Units{·µmol·l^-1};
  HH_OXIDATIVE_STRESS::EP_IN_VITRO_HMOX_OXIDATIVE_STRESS_NFOLD_NEG_CONTROL:
    result := Units{Real};
  HH_REPEATED_ORAL::EP_CELL_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_NUMBER_IN_
     BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_NUMBER_IN_BALF:
    result := Units{Real};
  HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_
     PERC_IN_BALF:
    result := Units{·%};
  HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF:
    result := Units{·%};
  HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF:
    result := Units{Real};
  HH_GENETIC_IN_VIVO::EP_DNA_STRAND_BREAKS:
    result := Units{·%};
  HH_BARRIER_INTEGRITY::EP_INVITRO_BARRIER_INTEGRITY:
    result := Units{Ω··cm^-2};
  HH_BARRIER_INTEGRITY::EP_TEER_DECREASE_VERSUS_CONTROL:
    result := Units{·%};
  HH_IMMUNOTOXICITY::EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION:
    result := Units{·pg·ml^-1}
  else
    /*result := Units{Real}*/end
```

```
function ENDPOINT_KB::EP_Units_X(ep_descriptor :: any Enumerate ):: Units
  case ep_descriptor of
    EP_DmPx_D1, EP_DmPx_D2, EP_DmPx_D3, EP_DnPx_D1, EP_DnPx_D2, EP_DnPx_D3, EP_DvPx_D1, EP_DvPx_D2, EP_DvPx_D3, EP_DsPx_D1, EP_DsPx_D2, EP_DsPx_D3, EP_DiPx_D1, EP_DiPx_D2, EP_DiPx_D3:
      result := Units{·%};
    EP_SPIN_COUNT_PER_SURFACE_CONC:
      result := Units{·m²·l⁻¹};
    EP_OXIDATIVE_DAMAGE_PER_DOSE:
      result := Units{·m²·l⁻¹, ·g·l⁻¹};
    EP_FRAS_SCORE_MASS:
      result := Units{·g·l⁻¹};
    EP_FRAS_SCORE_SURF:
      result := Units{·m²·l⁻¹};
    PC_GRANULOMETRY::EP_RELATIVE_INTENSITY:
      result := Units{·nm, ·µm};
    PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU, EP_DCFH_ROS_GENERATION_AU:
      result := Units{·mg·ml⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_OXIDATION_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_SCORE_MASS:
      result := Units{·µg·ml⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_MASS:
      result := Units{·mg·l⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_SURF:
      result := Units{·m²·l⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_MASS:
      result := Units{·mg·ml⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_SURF:
      result := Units{·mg·ml⁻¹};
    PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL:
      result := Units{·µg·cm⁻²};
    HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL, HH_OXIDATIVE_STRESS::EP_NRF2_LUCIFERASE_ACTIVITY, EP_NRF2_FOLD_LUCIFERASE_ACTIVITY_INDUCTION, HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_
      NM, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_NM, HH_OXIDATIVE_STRESS::EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN:
      result := Units{·µg·cm⁻²};
    EP_DCFH_AIR_LIQUID_INTERFACE_PERC_OF_CONTROL:
      result := Units{·ng·ml⁻¹};
    HH_GENETIC_IN_VITRO::EP_DNA_STRAND_BREAKS, HH_GENETIC_IN_VITRO::EP_FPG_SENSITIVE_SITES, HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_450_NM:
      result := Units{·µg·cm⁻², ·µg·ml⁻¹};
    HH_GENETIC_IN_VIVO::EP_DNA_STRAND_BREAKS:
      result := Units{·mg·kg⁻¹};
    EP_RESAZURIN_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_NORMALISED_POST_EXPOSURE_CELL_INDEX_1, HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL:
      result := Units{·µg·cm⁻²};
    HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_CFE_CYTOTOXICITY_PERC_
      OF_CONTROL, HH_BARRIER_INTEGRITY::EP_INVITRO_BARRIER_INTEGRITY:
      result := Units{·ng·ml⁻¹, ·µg·ml⁻¹};
    HH_CYTOTOXICITY::EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE:
      result := Units{·µg·cm⁻²};
    HH_IMMUNOTOXICITY::EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION, HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE:
      result := Units{·µg·ml⁻¹};
    HH_REPEATED_ORAL::EP_CELL_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_PERC_IN_BALF, HH_
      REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_
      NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_NUMBER_IN_BALF:
      result := Units{·mg·kg⁻¹};
    HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_
      NEUTROPHILS_NUMBER_IN_BALF:
      result := Units{·mg·kg⁻¹};
    HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx:
      result := Units{·d};
    EC_ALGAE_TOX::EP_GROWTH, EC_ALGAE_TOX::EP_YIELD, EC_ALGAE_TOX::EP_BIOMASS:
      result := Units{·%};
    EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION, EC_AQUATIC_INVERT_TOX_SHORT::EP_MORTALITY:
      result := Units{·%};
    EC_AQUATIC_INVERT_TOX_CHRONIC::EP_IMMOBILIZATION:
      result := Units{·%};
    EC_FISH_TOX_SHORT::EP_MORTALITY, EC_FISH_TOX_SHORT::EP_DEVELOPMENT, EC_FISH_TOX_SHORT::EP_LYSOSOMAL_INTEGRITY, EC_FISH_TOX_SHORT::EP_METABOLIC_ACTIVITY, EC_FISH_TOX_SHORT::EP_PLASMA_MEMBRANE_INTEGRITY:
      result := Units{·%};
    EC_FISH_TOX_CHRONIC::EP_HATCHING:
      result := Units{·%}
  end
```

```
function ENDPOINT_KB::EP_Units_T( ep_descriptor :: any Enumerate ):: Units
  case ep_descriptor of
    PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL:
      result := Units{·h};
    PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU, PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU:
      result := Units{·min};
    EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY:
      result := Units{·h};
    EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG:
      result := Units{·d};
    PC_WATER_SOL::EP_PERCENTAGE_DISSOLVED:
      result := Units{·min};
    EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION:
      result := Units{·h};
    HH_OXIDATIVE_STRESS::EP_CHANGE_IN_GSH_LEVEL:
      result := Units{·h};
    HH_BARRIER_INTEGRITY::EP_INVITRO_BARRIER_INTEGRITY:
      result := Units{·s, ·h, ·d};
    HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_NM, HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL:
      result := Units{·h}
  end
```

```
function ENDPOINT_KB::EP_Enums( ep_descriptor :: any Enumerate ):: Enumerates
  case ep_descriptor of
    PC_CLASSIFICATION_LABELING::CLP_HCODE, PC_CLASSIFICATION_LABELING::CLP_HCODE_GENERIC_CONC_LIMIT, PC_CLASSIFICATION_LABELING::CLP_HCODE_SPECIFIC_CONC_LIMIT, PC_CLASSIFICATION_LABELING::CLP_HCODE_M_FACTOR:
      result := GHS_KB::HCode→Enumerates;
    PC_CLASSIFICATION_LABELING::GHS_CODE:
      result := GHS_KB::GHSxx→Enumerates;
    PC_APPEARANCE::EP_PHYSICAL_STATE:
      result := MATERIAL_KB::PhysicalState→Enumerates;
    PC_APPEARANCE::EP_ODOUR:
      result := OdourCategory→Enumerates;
    PC_GRANULOMETRY::EP_DnPx_D1, EP_DnPx_D3, EP_ASPECT_RATIO_D1_D3, EP_ASPECT_RATIO_D3_D1, PC_GRANULOMETRY::EP_FERET_DIAMETER_D1, PC_GRANULOMETRY::EP_FERET_DIAMETER_D3:
      result := ParticleSizeLevel→Enumerates;
    PC_GRANULOMETRY::EP_DIMENSION:
      result := Dimension→Enumerates;
    PC_GRANULOMETRY::EP_OBSERVATION_SCALE:
      result := ObservationScale→Enumerates;
    PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP:
      result := MATERIAL_KB::SpaceGroup→Enumerates;
    PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM:
      result := MATERIAL_KB::CrystalSystem→Enumerates;
    PC_ASPECT_RATIO_SHAPE::EP_SHAPE_CATEGORY:
      result := MATERIAL_KB::ShapeCategory→Enumerates;
    PC_ASPECT_RATIO_SHAPE::EP_SHAPE_SUBCATEGORY:
      result := MATERIAL_KB::ShapeSubCategory→Enumerates;
    PC_ASPECT_RATIO_SHAPE::EP_ASSEMBLY_STRUCTURE_CP:
      result := MATERIAL_KB::AssemblyStructure→Enumerates;
    PC_ASPECT_RATIO_SHAPE::EP_ASSEMBLY_STRUCTURE_AGG:
      result := MATERIAL_KB::AssemblyStructure2nd→Enumerates;
    PC_COMPOSITION::EP_CONSTITUENT_ROLE:
      result := MATERIAL_KB::ConstituentRole→Enumerates;
    PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC, PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC:
      result := Atom→Enumerates;
    PC_COMPOSITION::EP_COMPOSITION_CATEGORY:
      result := CompositionCategory→Enumerates;
    HH_ACUTE_TOX_INHAL::EP_TOX_CATEGORY_STIS:
      result := ToxCategory→Enumerates;
    HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE, HH_IMMUNOTOXICITY::EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION:
      result := BM_CYTOKINES→Enumerates;
    HH_IMMUNOTOXICITY::EP_HEAT_SHOCK_PROTEIN_PERC_OF_CONTROL:
      result := BM_HEAT_SHOCK_PROTEINS→Enumerates;
    EC_FISH_TOX_SHORT::EP_LYSOSOMAL_INTEGRITY, EC_FISH_TOX_SHORT::EP_METABOLIC_ACTIVITY, EC_FISH_TOX_SHORT::EP_PLASMA_MEMBRANE_INTEGRITY:
      result := Enumerates{IC_x};
    EC_BAC_TOX::EP_GROWTH_INHIBITION, EC_BAC_TOX::EP_NITRIFICATION_INHIBITION, EC_BAC_TOX::EP_OXYGEN_CONSUMPTION:
      result := Enumerates{EC_x};
    EC_FISH_TOX_SHORT::EP_DEVELOPMENT:
      result := Enumerates{EC_x};
    EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION:
      result := Enumerates{EC_x};
    EC_FISH_TOX_SHORT::EP_MORTALITY:
      result := Enumerates{EC_x, LC_x};
    EC_FISH_TOX_CHRONIC::EP_SURVIVAL, EC_FISH_TOX_CHRONIC::EP_WEIGHT, EC_FISH_TOX_CHRONIC::EP_LENGTH, EC_FISH_TOX_CHRONIC::EP_ABNORMAL_APPEARANCE_AND_BEHAVIOR:
      result := Enumerates{EC_x};
    EC_FISH_TOX_CHRONIC::EP_HATCHING:
      result := Enumerates{EC_x, LC_x};
    EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION, EC_AQUATIC_INVERT_TOX_SHORT::EP_MORTALITY:
      result := Enumerates{EC_x, LC_x};
    EC_AQUATIC_INVERT_TOX_CHRONIC::EP_IMMOBILIZATION:
      result := Enumerates{EC_x};
    EC_ALGAE_TOX::EP_GROWTH, EC_ALGAE_TOX::EP_YIELD, EC_ALGAE_TOX::EP_BIOMASS:
      result := Enumerates{EC_x};
    EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION, EC_SEDIMENT_TOX::EP_SURVIVAL:
      result := Enumerates{EC_x};
    EC_SOIL_TOX::EP_SURVIVAL:
      result := Enumerates{LC_x};
    EC_SOIL_TOX::EP_REPRODUCTION:
      result := Enumerates{EC_x}
  end

function ENDPOINT_KB::EP_TextBased( ep_descriptor :: any Enumerate ):: Boolean
  case ep_descriptor of
    ID_CAS_REG_NR, ID_EC_REG_NR, ID_CHEMICAL_NAME, ID_IUPAC_NAME, ID_JRC_ID, ID_SMILES, ID_INCHIKEY, ID_INCHI, ID_EINECS, EP_MINERAL_NAME, EP_MOLECULAR_FORMULA, EP_COLOUR, PC_SURFACE_CHEMISTRY::EP_NOMINAL_INORGANIC_
      COMPOSITION, PC_SURFACE_CHEMISTRY::EP_NOMINAL_ORGANIC_COMPOSITION:
      result := True
  end
```

```
function ENDPOINT_KB::EP_DataType( ep_descriptor :: any Enumerate,data_op :: DataOperator ):: DataType
  if EP_Enums(ep_descriptor)→NotEmpty then
  begin
    if EP_Units_Y(ep_descriptor)→NotEmpty then
    begin
      if EP_Units_X(ep_descriptor)→NotEmpty then
      begin
        if EP_Units_T(ep_descriptor)→NotEmpty then
          result := ConvertDataType(tENUM_XYT, data_op)
        else
          result := ConvertDataType(tENUM_XY, data_op)
      end
      else
        if EP_Units_T(ep_descriptor)→NotEmpty then
          result := tENUM_YT
        else
          result := tENUM_Y
    end
    else
    begin
      /* Qualitative */    ;
      result := tENUM
    end
  end
  else
    if EP_Units_Y(ep_descriptor)→NotEmpty then
    begin
      if EP_Units_X(ep_descriptor)→NotEmpty then
      begin
        if EP_Units_T(ep_descriptor)→NotEmpty then
          result := ConvertDataType(tNUM_XYT, data_op)
        else
          result := ConvertDataType(tNUM_XY, data_op)
      end
      else
        if EP_Units_T(ep_descriptor)→NotEmpty then
          result := tNUM_YT
        else
          result := tNUM_Y
    end
    else
      if EP_TextBased(ep_descriptor) then
      begin
        /* Text based, either open or mask based. */      ;
        result := tTEXT
      end
```

```
function ENDPOINT_KB::EP_DataOperators(ep_descriptor :: any Enumerate,dt :: DataType,enum_y :: any Enumerate ):: DataOperators
  begin
    case dt of
      tNUM_Y, tENUM_Y:
        begin
          result := DataOperators{oNONE, oMEAN, oMEDIAN, oGEOMEAN, oMIN, oMAX}
        end;
      tNUM_XY:
        begin
          result := DataOperators{oNONE, oMEAN_XY}
        end;
      tNUM_X:
        begin
          result := DataOperators{oMODE, oMODE_2nd, oMODE_3th}
        end
      end;
        case ep_descriptor of
      CLP_HCODE_GENERIC_CONC_LIMIT, CLP_HCODE_SPECIFIC_CONC_LIMIT, CLP_HCODE_M_FACTOR:
        result := DataOperators{oNONE};
      EP_IN_VITRO_CYTOKINE_RELEASE:
        result := DataOperators{oLOAEC};
      PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_SURFACE:
        result := DataOperators{oAUC};
      HH_CYTOTOXICITY::EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE:
        result := DataOperators{oIC50};
      EC_FISH_TOX_SHORT::EP_MORTALITY, EC_FISH_TOX_SHORT::EP_DEVELOPMENT:
        begin
          if (enum_y = nil) or (enum_y = EC_x) then
            result := DataOperators{oNONE, oNOEC}
          else
            result := DataOperators{oNONE}
        end;
      EC_BAC_TOX::EP_GROWTH_INHIBITION, EC_BAC_TOX::EP_NITRIFICATION_INHIBITION, EC_BAC_TOX::EP_OXYGEN_CONSUMPTION:
        begin
          result := DataOperators{oNONE, oNOEC, oLOEC}
        end
    end

function ENDPOINT_KB::CheckValue_Y(dp : EP_DataObject,y : Unit ):: Boolean
|  CheckValue_Y_InDomain(dp.ep_rec.result_endpoint, dp.data_type, y) and CheckValue_Y_InRange(dp, y) and CheckValue_WithinConstraints(dp, y)


function ENDPOINT_KB::CheckValue_Y_InDomain(ep_descriptor :: any Enumerate,ep_qualifier :: DataType,v : Unit ):: Boolean
  case ep_descriptor of
    EP_PH, EP_ISOELECTRIC_POINT:
      result := (v→Unit as Real)→If((v as Real)→Condition(uv | (uv > -1) and (uv ≤ 15)), False);
    EP_ASPECT_RATIO_D1_D3, EP_ROUNDNESS, EP_SOLIDITY, EP_CIRCULARITY, PC_GRANULOMETRY::EP_DISPERSITY:
      result := (v→Unit as Real)→If((v as Real)→Condition(uv | (uv > 0) and (uv ≤ 1)), False);
    EP_ASPECT_RATIO_D3_D1:
      result := (v→Unit as Real)→If(v as Real ≥ 1, False);
    EP_TRUE_DENSITY, EP_ABSOLUTE_POWDER_DENSITY, EP_APPARENT_PARTICLE_DENSITY, EP_APPARENT_POWDER_DENSITY, EP_BULK_DENSITY, EP_EFFECTIVE_DENSITY, EP_ENVELOPE_DENSITY, EP_SKELETAL_DENSITY, EP_TAP_DENSITY, EP_
       THEORETICAL_DENSITY:
      result := (v→Unit as ·g·cm⁻³)→If((v as ·g·cm⁻³)→Condition(uv | (uv > 0.0·g·cm⁻³) and (uv < 23.0·g·cm⁻³)), False);
    PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA:
      result := (v→Unit as ·m²·g⁻¹)→If((v as ·m²·g⁻¹)→Condition(uv | (uv > 0.0·m²·g⁻¹) and (uv < 10000.0·m²·g⁻¹)), False);
    PC_GRANULOMETRY::EP_NOMINAL_DIAMETER, PC_GRANULOMETRY::EP_NOMINAL_LENGTH, EP_PRIMARY_PARTICLE_DIAMETER, EP_PRIMARY_PARTICLE_LENGTH, EP_FERET_DIAMETER_D1, EP_FERET_DIAMETER_D3, EP_LEGENDRE_ELLIPSE_D1, EP_LEGENDRE_
       ELLIPSE_D3, EP_GEODESIC_LENGTH_D3, EP_EQUIVALENT_CIRCLE_DIAMETER, EP_SURFACE_EQ_SPHERE_DIAMETER, EP_VOLUME_EQ_SPHERE_DIAMETER, EP_VOLUME_EQ_DISC_DIAMETER, EP_VOLUME_EQ_DISC_THICKNESS, EP_VOLUME_EQ_CYLINDER_
       DIAMETER, EP_VOLUME_EQ_CYLINDER_LENGTH, EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER, EP_Z_AVERAGE_DIAMETER, EP_STOKES_EQ_SPHERE_DIAMETER, EP_AERODYNAMIC_EQ_SPHERE_DIAMETER, EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER, EP_SIEVE_
       EQ_SPHERE_DIAMETER, EP_ELECTRICAL_MOBILITY_EQ_SPHERE_DIAMETER, EP_GEOMETRIC_MEAN_DIAMETER, EP_PRIMARY_PARTICLE_LENGTH, EP_DmPx_D1, EP_DmPx_D2, EP_DmPx_D3, EP_DnPx_D1, EP_DnPx_D2, EP_DnPx_D3, EP_DvPx_D1, EP_DvPx_
       D2, EP_DvPx_D3, EP_DsPx_D1, EP_DsPx_D2, EP_DsPx_D3, EP_DiPx_D1, EP_DiPx_D2, EP_DiPx_D3:
      result := (v→Unit as ·nm)→If((v as ·nm)→Condition(uv | (uv > 0.0·nm)), False);
    PC_COMPOSITION::EP_MASS_CONC, EP_CRYSTAL_SYSTEM, EP_SHAPE_CATEGORY, EP_SHAPE_SUBCATEGORY:
      result := (v→Unit as ·%)→If((v as ·%)→Condition(perc | ((perc ≥ 0.0·%) and (perc ≤ 100.0·%))), False)
    else
      result := True
  end
```

```
function ENDPOINT_KB::CheckValue_Y_InRange(dp : EP_DataObject,v : Unit ):: Boolean
  with dp.ep_rec | ep then
  begin
    with ep.dataobjects→Excluding(dp) | other_datapoints then
    begin
      /* Only datapoints of the same qualifier and replicate and same experiment are relevant */    ;
      with other_datapoints→Select(odp | Current(odp.valid) and (odp.data_type = dp.data_type) and (odp.replicate = dp.replicate) and (odp.experiment = dp.experiment) or (odp.material = dp.material)) | other_
        relevant_datapoints then
      begin
        case ep.result_endpoint of
          EP_CRYSTAL_SYSTEM, EP_SPACE_GROUP, EP_SHAPE_CATEGORY, EP_SHAPE_SUBCATEGORY:
            begin
              /* The total percentages of all enumerates may not exceed 100% */           ;
              with other_relevant_datapoints.value_y→Sum | total_others do
              begin
                if 100.0·% - total_others ≥ v then
                  result := True
              end
            end;
          EP_DmPx_D1, EP_DmPx_D2, EP_DmPx_D3, EP_DnPx_D1, EP_DnPx_D2, EP_DnPx_D3, EP_DvPx_D1, EP_DvPx_D2, EP_DvPx_D3, EP_DsPx_D1, EP_DsPx_D2, EP_DsPx_D3, EP_DiPx_D1, EP_DiPx_D2, EP_DiPx_D3:
            begin
              /* The size of lower percentiles may not exceed those of higher percentiles and visa versa */           ;
              with dp.value_x | x do
              begin
                result := True;
                with other_relevant_datapoints→Select(odp | Known(odp.value_x) and (dp.enum_y = odp.enum_y)) | other_known_datapoints then
                begin
                  if Known(dp.value_x) then
                  begin
                    with other_known_datapoints→Select(odp | odp.value_x > x) | higher_percentile_datapoints do
                      result := higher_percentile_datapoints→ForAll(odp | (not Known(odp.value_y)) or (odp.value_y > v))                ;
                    if result then
                      with other_known_datapoints→Select(odp | odp.value_x < x) | lower_percentile_datapoints do
                        result := lower_percentile_datapoints→ForAll(odp | (not Known(odp.value_y)) or (odp.value_y < v))
                  end
                end
              end
            end
          else
            begin
              /* There are no other datapoints for the same replicate to take into account. */           ;
              result := True
            end
        end
      end
      else
      begin
        result := True
      end
    end
    else
    begin
      /* There are no other datapoints to take into account. */    ;
      result := True
    end
  end

function ENDPOINT_KB::CheckEnum_Y(dp : EP_DataObject,e :: any Enumerate ):: Boolean
| (CheckEnum_Y_InDomain(dp, e) and CheckEnum_Y_InRange(dp, e))
```

```
function ENDPOINT_KB::Enum_Y_Domain(dp : EP_DataObject) :: Enumerates
  with dp.ep_rec | ep then
  begin
    case ep.result_endpoint of
      EP_CONSTITUENT_ROLE:
        begin
          if ep.rec_owner is CandidateNFProxy | cp then
          begin
            /* TO DO VNR */
          end
          else
            if ep.rec_owner is MaterialProxy | mp then
            begin
              /* */
            end
            else
              if ep.rec_owner is Material | m then
                result := m.ConstituentRoleDomain(m.composer)
        end;
      EP_SPACE_GROUP:
        begin
          if ep.rec_owner is CrystallinePhase | cr_phase then
          begin
            result := cr_phase.SpaceGroupDomain()
          end
          else
            result := SpaceGroup→Enumerates
        end
      else
        result := EP_Enums(ep.result_endpoint)
    end
  end

function ENDPOINT_KB::CheckEnum_Y_InDomain(dp : EP_DataObject, e :: any Enumerate) :: Boolean
| e in Enum_Y_Domain(dp)

function ENDPOINT_KB::CheckEnum_Y_InRange(dp : EP_DataObject, e :: any Enumerate) :: Boolean
| e in Enum_Y_Range(dp)

function ENDPOINT_KB::CheckText_InDomain(dp : EP_DataObject, t : String) :: Boolean
  with dp.ep_rec | ep then
  begin
    case ep.result_endpoint of
      PC_IDENTITY::ID_CAS_REG_NR:
        result := (t = "") or IsValidCASnumber(t)
      else
        result := True
    end
  end
  else
    result := True

function ENDPOINT_KB::CheckValue_X(dp : EP_DataObject, x : Unit) :: Boolean
| CheckValue_X_InDomain(dp.ep_rec.result_endpoint, x)

function ENDPOINT_KB::CheckValue_X_InDomain(ep_descriptor :: any Enumerate, v : Unit) :: Boolean
  case ep_descriptor of
    EP_DmPx_D1, EP_DmPx_D2, EP_DmPx_D3, EP_DnPx_D1, EP_DnPx_D2, EP_DnPx_D3, EP_DvPx_D1, EP_DvPx_D2, EP_DvPx_D3, EP_DsPx_D1, EP_DsPx_D2, EP_DsPx_D3, EP_DiPx_D1, EP_DiPx_D2, EP_DiPx_D3:
      result := (v→Unit as ·%)→If((v as ·%)→Condition(perc | ((perc ≥ 0.0·%) and (perc ≤ 100.0·%))), False)
    else
      result := True
  end
```

```
function ENDPOINT_KB::CheckValue_WithinConstraints(dp : EP_DataObject,v : Unit ):: Boolean
  with dp.ep_rec | ep_rec then
  begin
    with ep_rec.rec_owner→If(ro | ro.endpoints→Excluding(ep_rec), ep_rec.rec_owner→If(a | a.endpoints→Excluding(ep_rec), EP_Records{})) | other_endpoint_records then
    begin
      with other_endpoint_records.dataobjects→Sum | other_dps then
      begin
        with EndpointsConstraint→Leaves | constraint_classes then
          result := constraint_classes→ForAll(cc | cc.WithinConstrains(dp, other_dps, v))
        else
          result := True
      end
      else
        result := True
    end
    else
      result := True
  end
  else
    result := True


function ENDPOINT_KB::EPQ(ep :: any Enumerate ):: EP_Qualifier
  begin
    result := EP_Qualifier→New;
    result.endpoint_descriptor := ep
  end


function ENDPOINT_KB::EPQM(ep :: any Enumerate,med :: MediumDescriptor ):: EP_Qualifier
  begin
    result := EP_Qualifier→New;
    result.endpoint_descriptor := ep;
    result.medium_qualifier := med
  end


function ENDPOINT_KB::EPQMA(ep :: any Enumerate,med :: MediumDescriptor,assay :: AssayDescriptor ):: EP_Qualifier
  begin
    result := EP_Qualifier→New;
    result.endpoint_descriptor := ep;
    result.medium_qualifier := med;
    result.assay_descriptor := assay
  end


function ENDPOINT_KB::EPQU(ep :: any Enumerate,unit :: Unit ):: EP_Qualifier
  begin
    result := EP_Qualifier→New;
    result.endpoint_descriptor := ep;
    result.v_unit ?= unit
  end


function ENDPOINT_KB::EDIT(epq : EP_Qualifier ):: EP_Qualifier
  begin
    result := epq;
    result.edit := True
  end


function ENDPOINT_KB::OP(epq : EP_Qualifier,op :: DataOperator ):: EP_Qualifier
  begin
    result := epq;
    result.v_operator := op
  end


function ENDPOINT_KB::WTG(epq : EP_Qualifier ):: EP_Qualifier
  begin
    epq.section := sWTG;
    result := epq
  end
```

```
function ENDPOINT_KB::WTD( epq : EP_Qualifier ) :: EP_Qualifier
  begin
    epq.section := sWTD;
    result := epq
  end

function ENDPOINT_KB::PER( epq : EP_Qualifier, per_x : Quantity ) :: EP_Qualifier
  begin
    result := epq;
    result.per_x := per_x
  end

function ENDPOINT_KB::CELL( epq : EP_Qualifier, cell :: any Enumerate ) :: EP_Qualifier
  begin
    result := epq;
    result.cell_qualifier := cell
  end

function ENDPOINT_KB::MED( epq : EP_Qualifier, med :: any Enumerate ) :: EP_Qualifier
  begin
    result := epq;
    result.medium_qualifier := med
  end

function ENDPOINT_KB::ENUM( epq : EP_Qualifier, enum :: any Enumerate ) :: EP_Qualifier
  begin
    result := epq;
    result.enum := enum
  end

function ENDPOINT_KB::MEAS( epq : EP_Qualifier ) :: EP_Qualifier
  begin
    result := epq;
    result.source_type := sMeasured
  end

function ENDPOINT_KB::ASSAY( epq : EP_Qualifier, assay_descriptor :: AssayDescriptor ) :: EP_Qualifier
  begin
    result := epq;
    result.assay_descriptor := assay_descriptor
  end

function ENDPOINT_KB::DUR( epq : EP_Qualifier, t : Time ) :: EP_Qualifier
  begin
    result := epq;
    result.at_t := t
  end

function ENDPOINT_KB::TITLE( str : String, epq : EP_Qualifier ) :: EP_Qualifier
  begin
    result := epq;
    result.title := str
  end
```

```
function ENDPOINT_KB::Datapoint_FromAssays(assays : Assays,epq : EP_Qualifier ):: EP_DataObject
  with assays.endpoints→Sum→Select(rec | rec.MatchesQualifier(epq)) | all_records then
  begin
    if all_records→Size = 1 then
    begin
      /*  */    ;
      result := all_records[1].DeriveQualified_Datapoint(epq)
    end
    else
      with EP_Datapoints{} | datapoints do
      begin
        foreach rec of all_records do
        begin
          with rec.DeriveQualified_Datapoint(epq) | dp then
            datapoints→Add(dp)
        end;
        if datapoints→Size = 1 then
          result := datapoints[1]
        else
          if datapoints→Size > 1 then
          begin
            result := EP_DataObject→New;
            result.endpoint_qualifier ?= epq;
            result.valid := True;
            result.source_dps := datapoints;
            result.enum_y := epq.enum;
            result.value_x := epq.per_x;
            result.value_y := datapoints.value_y→Average;
            result.distr_type_y := dqSD;
            result.distr_y := datapoints.value_y→StdDev
          end
      end
  end

function ENDPOINT_KB::Datapoint_FromEndpointRecords(endpoint_records : EP_Records,epq : EP_Qualifier ):: EP_DataObject
  with endpoint_records→Select(r | r.MatchesQualifier(epq)) | qualified_records then
  begin
    if qualified_records→Size = 1 then
    begin
      /*  */    ;
      result := qualified_records[1].DeriveQualified_Datapoint(epq)
    end
    else
      with EP_Datapoints{} | datapoints do
      begin
        foreach rec of qualified_records do
        begin
          with rec.DeriveQualified_Datapoint(epq) | dp then
            datapoints→Add(dp)
        end;
        if datapoints→Size = 1 then
          result := datapoints[1]
        else
          if datapoints→Size > 1 then
          begin
            result := EP_DataObject→New;
            result.endpoint_qualifier ?= epq;
            result.valid := True;
            result.source_dps := datapoints;
            result.value_x := epq.per_x;
            result.value_y := datapoints.value_y→Average;
            result.distr_type_y := dqSD;
            result.distr_y := datapoints.value_y→StdDev
          end
      end
  end
```

```
function ENDPOINT_KB::MapStrEnum(str : String,ep :: any Enumerate ):: any Enumerate
  with str→Trim | txt do
  begin
    case ep of
      PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC, PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC:
        begin
          result := Atom→Enumerates→Any(en | en→Name = txt)
          end;
          PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP:
          case str of
          "Amorphous", "amorphous":
          result := SpaceGroup[231];
          "Rutile", "rutile":
          result := SpaceGroup[136];
          "Anatase", "anatase":
          result := SpaceGroup[141];
          "Brookite", "brookite":
          result := SpaceGroup[61]
        end;
      HH_ACUTE_TOX_INHAL::EP_TOX_CATEGORY_STIS:
        begin
          result := ToxCategory→Enumerates→Any(cat | cat→Name = txt)
        end
    end
  end


function ENDPOINT_KB::EnumToStr(enum :: any Enumerate ):: String
  if enum ≠ nil then
  begin
    with enum→Enumeration | enumeration then
    begin
      case enumeration of
        GHS_KB::HCode:
          result := GHS_KB::HPhraseToStr(enum);
        SpaceGroup:
          result := MATERIAL_KB::SpaceGroupToStr(enum);
        ShapeCategory:
          result := MATERIAL_KB::ShapeCategoryToStr(enum);
        ParticleSizeLevel:
          result := ParticleSizeLevelToStr(enum);
        DataOperator:
          result := DataOperatorToStr(enum)
        else
          result := enum→AsString
      end
    end
  end
  else
    result := "?"


function ENDPOINT_KB::Convertors(dest_epq : EP_Qualifier ):: ConvertorClasses
  with EndpointConvertor→Leaves→AsSequence | convertors then
  begin
    result := convertors→Select(cv | cv.MatchConversionEndpoint(dest_epq))
  end


function ENDPOINT_KB::Calculators(dest_epq : EP_Qualifier ):: CalculatorClasses
  with EndpointCalculator→Leaves→AsSequence | calculators then
  begin
    result := calculators→Select(cl | cl.MatchCalculationEndpoint(dest_epq))
  end
```

```
function ENDPOINT_KB::DistrQualifierToStr( dq :: DistrQualifier ) :: String
  case dq of
    dqNO:
      result := "none";
    dqPLUS_MIN:
      result := "±";
    dqRSD_PERC:
      result := "rsd%";
    dqSD:
      result := "sd";
    dqGEOSD:
      result := "geosd"
  end
```

```
function ENDPOINT_KB::MapDistrQualifierUnit( dq :: DistrQualifier, v_unit :: Unit ) :: Unit
  case dq of
    dqRSD_PERC:
      result := ·%
    else
      result := (v_unit ≠ nil)→If(v_unit, Real)
  end
```

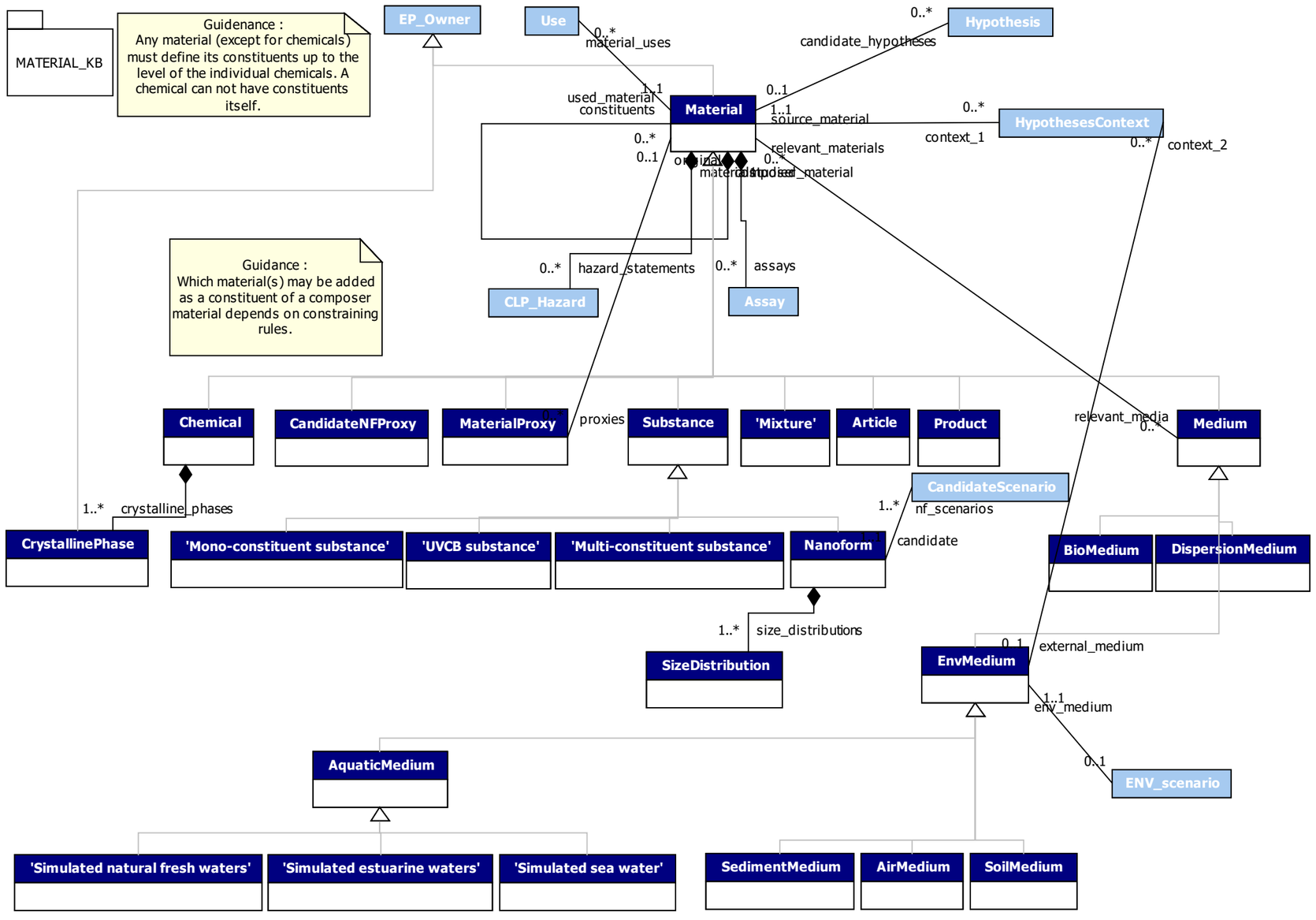
```
function ENDPOINT_KB::ConvertDataType( src_dt :: DataType, dop :: DataOperator ) :: DataType
```

C1	src_dt	tNUM_XY			tENUM_XY			tNUM_XYT			ELSE	
C2	dop	oMEAN, oMEDIAN, oPEAK, oPEAK_2nd, oPEAK_3th, oAUC, oSLOPE	oMODE, oMODE_2nd, oMODE_3th, oIC10, oIC50, oEC50	ELSE	oMEAN, oMEDIAN, oPEAK,oPEAK_2nd, oPEAK_3th, oAUC, oSLOPE, oNOEC, oLOEC	oMODE, oMODE_2nd, oMODE_3th,oIC10, oIC50, oEC50	ELSE	oMEAN, oMEDIAN, oPEAK, oPEAK_2nd, oPEAK_3th, oAUC, oSLOPE	oMODE, oMODE_2nd, oMODE_3th, oIC10, oIC50, oEC50	ELSE	-	
A1	result	tNUM_Y	tNUM_X	src_dt	tENUM_Y	tENUM_X	src_dt	tNUM_YT	tNUM_XT	src_dt	src_dt	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	

```
function ENDPOINT_KB::Derive_DataRelevance( epq : EP_Qualifier ):: RelevanceObj
  case epq.endpoint_descriptor of
    PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME:
      begin
        case epq.medium_qualifier of
          'Simulated lung macrophage phagolysosomal fluid':
            begin
              result := RelevanceObj→New;
              result.measurable_min := 5.0·min;
              result.measurable_max := 1.0·a;
              result.bio_relevance_min := 10.0·min;
              result.bio_relevance_max := 60.0·d;
              result.match_threshold := 3;
              result.nomatch_threshold := 5
            end
        end
      end;
    PC_DUSTINESS::EP_RESPIRABLE_DUST_INDEX_MASS:
      begin
        result := RelevanceObj→New;
        result.measurable_min := 10.0·mg·kg⁻¹;
        result.measurable_max := 1000000.0·mg·kg⁻¹;
        result.bio_relevance_min := 10.0·mg·kg⁻¹;
        result.bio_relevance_max := 5000.0·mg·kg⁻¹;
        result.match_threshold := 5;
        result.nomatch_threshold := 5
      end;
    PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE:
      begin
        result := RelevanceObj→New;
        result.measurable_min := 0.2·nmol·mg⁻¹;
        result.measurable_max := 10000.0·nmol·mg⁻¹;
        /* neg control BaSO4 */      ;
        result.bio_relevance_min := 0.3·nmol·mg⁻¹;
        /* pos control CuO */      ;
        result.bio_relevance_max := 310.0·nmol·mg⁻¹;
        result.match_threshold := 5;
        result.nomatch_threshold := 5
      end;
    HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE:
      begin
        if epq.enum = BM_CYTOKINES::'LDH' then
        begin
          result := RelevanceObj→New;
          /*result.measurable_min := */        ;
          result.measurable_max := 180.0·µg·ml⁻¹;
          /* pos control CuO */        ;
          result.bio_relevance_min := 2.8·µg·ml⁻¹;
          /* valid dose range */        ;
          result.bio_relevance_max := 180.0·µg·ml⁻¹;
          result.match_threshold := 3;
          result.nomatch_threshold := 3
        end
      end
  end

function ENDPOINT_KB::EP_DistrTypes( ep_descriptor :: any Enumerate ):: DistributionTypes
  case ep_descriptor of
    PC_GRANULOMETRY::EP_DnPx_D1:
      result := Enumerates{}
    else
      result := Enumerates{dqNO, dqSD, dqPLUS_MIN}
  end
```

Chapter 4 MATERIAL_KB



4.1 Defined enumerations

`ConstituentRole`

Indicates the 'role' of a constituent material in relationship to its composing material. Which roles a constituent may have depends on properties of both the constituent itself and the composer.

- `'core'`
  A 'solid?' 'chemical' representing a substantial part of or the entire 'core' chemistry of a non hollow 'nano-object' (e.g. 'spheres', 'platelets', 'discs', 'rods', 'wires', 'cubes').
- `'shell'`
  A 'chemical' surrounding a 'core' or other 'shell'. (not yet clearly distinguished by definition from 'coating')

- 'coating'
  A 'chemical' surrounding either a 'core', 'wall', 'shell', 'coating' or 'aggregated' or 'agglomerated'
  WIKIPEDIA
  Functionalization is the introduction of organic molecules or polymers on the surface of the nanoparticle. The surface coating of nanoparticles determines many of their physical and chemical properties, notably stability, solubility, and targeting. A coating that is multivalent or polymeric confers high stability. Functionalized nanomaterial-based catalysts can be used for catalysis of many known organic reactions.
- 'corona'
  A protein based coating.. (to be deprecated as role) as this overlaps with coating.
- 'wall'
  A 'chemical' acting as a single or multiple 'walls' in a nanotube. (eg. SWCNT, MWCNT)
  Wall (the chemical of a tube)
- 'solid matrix'
  A solid material representing the matrix material of a composite potentially hosting/containing other dispersed materials.
- 'liquid medium'
  A liquid substance being the dominant material potentially containing other dispersed, dissolved materials.
  Liquid medium (a liquid representing the host medium of a suspension, dispersion, etc.)
- 'gaseous medium'
  A gaseous substance being the dominant material potentially containing other materials dispersed in it (like aerosols)
  Gaseous medium (a gas representing the host gaseous medium of an aerosol, etc.)
- 'substrate'
  A solid substance acting as the 'substrate' for another material in roles like: 'film', 'structured film', 'surface bound', 'surface').
  Substrate (a solid representing the substrate of film, structured film, etc.)
- 'surface'
  A layer of material attached to a substrate material
- 'film'
  Film (a very thin homogenous layer attached to a substrate material)
- 'structured film'
  Structured film (a very thin structured layer attached to a substrate material)
- 'surface bound'
  Surface bound (particulate matter bound to a surface)
- 'dispersed'
  Dispersed (particulate matter dispersed in a solid or liquid medium or gaseous medium (aerosol))
- 'dissolved'
  Dissolved (dissolved chemical in a liquid or solid medium)
- 'mixed'
  Mixed (a material mixed with other mixed materials)
- 'layered'
  Layered (a solid layer, layered with other layers) (eg. laminate)
- 'aggregated'
  Aggregated (strongly bounded with other particles)
- 'agglomerated'
  Agglomerated (weakly bounded with other particles)
- 'impurity'
  An unintended chemical being part of the composing material (eg. contaminant)
- 'contaminant'
  Deprecated (impurity only)
- 'container'
  Container (a substance, containing other materials, substances (glass of a bottle))
- 'contained'
  Contained (the material/substance/chemical contained by a container material)
- 'product'
- 'capsule'
  Capsule (a substance/chemical the capsule wall is made of)
- 'encapsulated'
  Encapsulated (a substance/chemical inside the capsule wall)
- 'dope'
  An intentional introduced impurity to alter certain material properties like electrical or optical properties (new..)
- 'additive'
  Constituent which is intentionally added to stabilise the substance and only for this purpose
- 'main chemical'
  A chemical representing the main constituent of a substance

PhysicalState

'Depending on the 'material-class' up to five 'states' are available: 'ions', 'solid', 'liquid', 'gas' and 'mixture'. Besides the three most common phases of matter: 'solid', 'liquid', 'gas' two other 'states' are added. 'Ions' representing matter in its ionic form either positive or negative charged and 'mixtures' representing the state of combinations of matter in different phases. The state 'mixture' can only occur if a 'substance' is composed of other 'substances' in different states.
IUCLID phrasegroup = A19

- `ions`
  Used to indicate that matter is in its ionic state. eg. Ag+
- `solid`
  Used to indicate the substance and all of its constituents are in solid phase. (eg. Ag(s))
  [2381]
- `liquid`
  Used to indicate a substance is in liquid state. (e.g. H2O(aq))
  [2038]
- `gas`
  Used to indicate a substance is in gaseous state. (e.g. CO2(g))
  [2830]
- `'mixed state'`
  The mixed state can only occur if a 'substance' is composed of other 'substances' in different states.

NanomaterialOrigin

ISO/TS 80004-1:2015
('natural') added by ThinkWorks

- `'engineered'`
  Designed for specific purpose of function
- `'manufactured'`
  Intentionally produced to have selected properties or composition.
- `'incidental'`
  Generated as an unintentional by-product of a process
- `'natural'`
  Generated/transformed by natural/environmental processes (not in ISO but in EC definition)

NOShape

IUCLID picklist?? => {flake, irregular, prismatic, rod, spherical, tubular, other}

- `'clusters'`
- `'dots'`
- `'wires'`
- `'rods'`
- `'tubes'`
- `'platelets'`
- `'disks'`
- `'spheres'`
- `'cubes'`

CoatingOrigin

Indicates the origin of the specific coating/shell. Multiple coatings/shells may exist each with its own origin.

- `'engineered'`
  Intentionally functionalized to alter one or more properties/functionalities of the coated nanomaterial
- `'from matrix'`
  an unintended coating due to degradation of the matrix still containing the NOAA. (eg. paint particles due to sanding containg nano-particles) (check?)
- `'from environment'`
  a (unintended?) coating as a result of environmental chemical processes. (eg. Ag2S(s) NP)
- `'biological'`
  a (unintended) coating due to biological interaction.

CompositionCategory

ThinkWorks introduced

- 'organic compound'
  An organic compound is generally any 'chemical' that contains carbon.
- 'organic matter'
  Organic matter is matter composed of organic compounds.
- 'inorganic compound'
  An inorganic compound is generally any chemical lacking carbon, so not an 'organic compound' or water.
- 'inorganic matter'
  Inorganic matter is matter composed of solely inorganic compounds.
- 'hybrid material'
  Hybrid materials are composites consisting of two or more 'chemicals' at the nanometer or molecular level, at least one being 'organic'. (Wikipedia)
- 'mixture'
  any combination of different material categories (eg.) above the nano or molecular size.
- 'water'

CrystalSystem

NM 21

- 'amorphous'
- 'triclinic'
  http://purl.enanomapper.org/onto/ENM_9000022
  [58271]
- 'monoclinic'
  http://purl.enanomapper.org/onto/ENM_9000029
  [58272]
- 'orthorhombic'
  http://purl.enanomapper.org/onto/ENM_9000031
  [58273]
- 'tetragonal'
  http://purl.enanomapper.org/onto/ENM_9000032
  [58274]
- 'trigonal'
  http://purl.enanomapper.org/onto/ENM_9000033
  [58275]
- 'hexagonal'
  http://purl.enanomapper.org/onto/ENM_9000034
  [58276]
- 'cubic'
  http://purl.enanomapper.org/onto/ENM_9000035
  [58277]

SubstanceCategory

See also, https://en.wikipedia.org/wiki/Mixture (extended with 'gas', 'liquid', 'solid', 'composite' , 'capsule' and 'none')
When dispersing NOAA's (Nano-Objects, Aggregates and Agglomerates) in the different continuous media the categories will become nano-enabled and map onto the ISO80004_Categories.

- 'gas'
  single continuous gas
- 'liquid'
  single continuous liquid
- 'solid'
  single continuous solid
- 'powder'
  a heterogenous mixture of colloidal and/or coarse particulate solids < 100 µm (eg, suger powder)
- 'gas mixture'
  homogeneous mixture of different gases (eg. air)
- 'liquid solution'
  a gas, liquid or solid dissolved in another continuous liquid medium (eg. oxygen in water, alcoholic beverages, sugar in water)
- 'aerosol'
  liquid colloid between 1 nm and 1 µm dispersed in a gas (eg. fog, mist, vapor, hair sprays)

- 'fluid foam'
  colloidal or coarse gas (bubbles) in a continuous liquid medium (e.g. whipped cream, shaving cream)
- 'emulsion'
  (colloidal or larger) liquid dispersed in another continuous liquid medium (eg. milk, mayonnaise, hand cream)
- 'sol'
  a colloidal solid dispersed in a continuous liquid medium (eg, pigmented ink, blood)
- 'solid foam'
  colloidal gas dispersed in a continuous solid medium (eg. aerogel, styrofoam, pumice)
- 'gel'
  a colloidal liquid dispersed in a continuous solid medium (eg. agar, gelatin,silicagel)
- 'solid sol'
  a colloidal solid dispersed in another solid continuous medium (eg, cranberry glass)
- 'solid aerosol'
  solid colloid between 1 nm and 1 µm dispersed in a gas (eg. smoke, nano and ultra fine powder)
- 'solid aerosol, dust'
  coarse solid exceeding 1 µm dispersed in a gas (eg. dust, superfine powder, granular powder)
- 'suspension'
  a coarse dispersion of a solid in a continuous liquid medium (eg, mud, chalk powder suspended in water)
- 'solid mixture'
  a heterogenous mixture of a coarse solid mixed with another solid (eg, gravel)
- 'composite'
  a heterogenous mixture of colloidal or coarse solids dispersed in another solid continuous medium (eg, cranberry glass, granite)
- 'solid solution'
  a gas, liquid or solid dissolved in another continuous solid medium (eg. hydrogen in metals, amalgam, hexane in parraffin wax)
- 'capsule'
- 'none'

LiquidCategory
- 'mist'
- 'droplets'
- 'fluid'

ViscosityCategory
- 'water-like'
  low, like water (< 1 cP)
- 'oil-like'
  medium, like oil (~100 cP)
- 'paste-like'
  high, like paste (> 1000 cP)

SolidSizeCategory
- 'solid object'
  solid object (> 10 mm)
- 'broken solid'
  broken solid (3 - 10 mm)
- 'granular solid'
  granular solid (0.1 - 3 mm)
- 'granular powder'
  granular powder (10 - 100 µm)
- 'superfine powder'
  superfine powder (1 - 10 µm)
- 'ultrafine powder'
  ultrafine powder (100 nm - 1 µm)
- 'nano powder'
  nanoscaled particles (1 nm - 100 nm)

NanoscaleDimensionality
- '0D'
  0D, no external dimensions in the nanoscale ~[1..100nm]

- '1D'
  1D, one external dimension in the nanoscale ~[1..100nm], the two others are significantly larger
- '2D'
  2D, two external dimensions in the nanoscale ~[1..100nm], the third significantly larger
- '3D'
  3D, all three external dimensions in the nanoscale ~[1..100nm]

PhaseSize

- continuous
  no particles in medium
- dissolved
  particle size (< 1 nm)
- colloid
  particle size (1 nm – 1 µm)
- coarse
  particle size (> 1 µm)

FlowType

- laminar
  Laminar flow (or streamline flow) occurs when a fluid flows in parallel layers, with no disruption between the layers.[1] At low velocities, the fluid tends to flow without lateral mixing, and adjacent layers slide past one another like playing cards.
- transitional
  A flow in which the viscous and Reynolds stresses are of approximately equal magnitude. It is transitional between laminar flow and turbulent flow.
- turbulent
  Turbulent flow, type of fluid (gas or liquid) flow in which the fluid undergoes irregular fluctuations, or mixing, in contrast to laminar flow, in which the fluid moves in smooth paths or layers.

CompactionClass

Soil compaction class.

- low
  packing_density < 1.4
- medium
  packing density ≥ 1.4 and < 1.75
- high
  packing density > 1.75

ISO80004_Category

An ISO nanomaterial is considered to be either a NANO-OBJECT or a NANOSTRUCTURED MATERIAL as defined by the ISO/TS 80004-1:2011

- 'nanomaterial'
  Material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale. [SOURCE: ISO/TS 80004 -1:2011, definition 2.3]
- 'nano-object'
  Material with one, two or three external dimensions in the nanoscale. [SOURCE: ISO/TS 80004 - 1:2011, definition 2.2]
- 'nano-particle'
  Nano-object (2.2) with all three external dimensions in the nanoscale (2.1) [SOURCE: ISO/TS 80004 - 1:2011, definition 2.4]
- 'nanofibre'
  Nano-object (2.2) with two similar external dimensions in the nanoscale (2.1) and the third dimension significantly larger. [SOURCE: ISO/TS 80004 - 1:2011, definition 2.5]
- 'nanoplate'
  Nano-object (2.2) with one external dimension in the nanoscale (2.1) and the two other external dimensions significantly larger. [SOURCE: ISO/TS 80004 - 1:2011, definition 2.5]
- 'nanostructured material'
  Material having internal or surface structure in the nanoscale. [SOURCE: ISO/TS 80004 -1:2011, definition 2.11]
- 'nanostructured powder'
  Powder comprising nanostructured agglomerates (3.1.2), nanostructured aggregates (3.1.1), or other particles of nanostructured material (2.11) [SOURCE: ISO/TS 80004 -1:2011, definition 3.1]
- 'nanostructured aggregate'
  Aggregate (2.7) formed from nano-objects (2.2) [SOURCE: ISO/TS 80004 -1:2011, definition 3.1.1]
- 'nanostructured agglomerate'
  Agglomerate (2.8) of nano-objects (2.2), or agglomerate of nanostructured (2.10) aggregates (2.7). [SOURCE: ISO/TS 80004 -1:2011, definition 3.1.2]
- 'nanostructured core-shell particle'
  Particle consisting of a core and shell(s), where the diameter of the core or the thickness of the shell is in the nanoscale (2.1) [SOURCE: ISO/TS 80004 -1:2011, definition 3.1.3]
- 'nanocomposite'
  Solid comprising a mixture of two or more phase-separated materials, one or more being nanophase (2.12) [SOURCE: ISO/TS 80004 -1:2011, definition 3.2]

- 'solid nanofoam'
  Solid matrix filled with a second, gaseous phase, typically resulting in a material of much lower density, with a nanostructured (2.10) matrix, for example having nanoscale (2.1) struts and walls, or gaseous nanophase (2.12) consisting of nanoscale bubbles [closed nanofoam (2.15)], or both [SOURCE: ISO/TS 80004 -1:2011, definition 3.3]
- 'nanoporous material'
  Solid material with nanopores (2.13) [SOURCE: ISO/TS 80004 -1:2011, definition 3.4]
- 'fluid nanodispersion'
  Heterogeneous material in which nano-objects (2.2) or a nanophase (2.12) are dispersed in a continuous fluid phase of a different composition. [SOURCE: ISO/TS 80004 -1:2011, definition 3.5]
- 'nanosuspension'
  Fluid nanodispersion (3.5) where the dispersed phase is a solid. [SOURCE: ISO/TS 80004 -1:2011, definition 3.5.1]
- 'nano-emulsion'
  Fluid nanodispersion (3.5) with at least one liquid nanophase (2.12). [SOURCE: ISO/TS 80004 -1:2011, definition 3.5.2]
- 'liquid nanofoam'
  Fluid nanodispersion (3.5) filled with a second, gaseous nanophase (2.12), typically resulting in a material of much lower density. [SOURCE: ISO/TS 80004 -1:2011, definition 3.5.3]
- 'nano aerosol'
  Fluid nanodispersion (3.5) with gaseous matrix and at least one liquid or solid nanophase (2.12) [including nano-objects (2.2)] [SOURCE: ISO/TS 80004 -1:2011, definition 3.5.4]

MaterialFunction

Indicates the intended function of the material or as constituent. Multiple functions per material are allowed.
Relevant for safer by design. Still needs to be extended with other functions.

- 'antimicrobial agent'
  the material has antimicrobial properties.
  http://purl.obolibrary.org/obo/CHEBI_33281
- 'bulk'
- 'binder'
  A 'binder' or binding agent is any 'material' or 'substance' that holds or draws other materials together to form a cohesive whole mechanically, chemically, by adhesion or cohesion.
  http://purl.enanomapper.org/onto/ENM_8000174
- 'catalyst'
  A catalysis is a chemical that increases the rate of a chemical reaction due to the participation, which is not consumed in the catalyzed reaction and can continue to act repeatedly. Often only tiny amounts of catalyst are required in principle.
  http://purl.obolibrary.org/obo/CHEBI_35223
- 'electrical conductor'
  a material allowing the flow of an electric charge
- 'decontaminant'
- 'dispersant'
  A dispersant or a dispersing agent or a plasticizer or a superplasticizer is either a non-surface active polymer or a surface-active substance added to a suspension, usually a colloid, to improve the separation of particles and to prevent settling or clumping. Dispersants consist normally of one or more surfactants.
- 'solvent'
  A 'solvent' is a substance that dissolves a 'solute' (a chemically distinct liquid, solid or gas), resulting in a solution. A solvent is usually a liquid but can also be a solid, a gas, or a supercritical fluid.
- 'pigment'
  A 'pigment' is a material that changes the color of reflected or transmitted light as the result of wavelength-selective absorption.
- 'preservative'
  A 'preservative' is a substance or a chemical that is added to various products like food, beverages, pharmaceutical drugs, paints, biological samples, cosmetics, wood and many other products to prevent decomposition by microbial growth or by undesirable chemical changes.
- 'substance studied'
  Indicates that this material batch is the subject in an assay like a 'toxicity study'.
- 'test vehicle'
  Indicates that this substance is used as a vehicle or carrier for the 'substance studied'.
- 'wetting agent'
- 'uv filter'
  An UV filter is a material that blocks or absorbs ultraviolet (UV) light.
- 'thickening agent'
  A thickening agent or thickener is a substance which can increase the viscosity of a liquid without substantially changing its other properties. Thickeners may also improve the suspension of other ingredients or emulsions which increases the stability of the product.
- 'anticaking agent'
  An anticaking agent is an additive placed in powdered or granulated materials to prevent the formation of lumps (caking).
  http://purl.obolibrary.org/obo/CHEBI_77964
- 'reinforcement filler'
- 'photocatalyst'
- 'self-cleaning agent'
- 'other'
  Other material functions not yet covered.. Please report new functions!

SizeType

- 'particle size'
  Represents the physical sizes of the particle in three dimensions. It is the primary size in case the particle is a Nano-object.
- 'Feret diameter'
  Feret's diameter (maximum distance edge to edge);
- 'volume equivalent sphere diameter'
  D_volume = diameter of a sphere with the same volume as the particle
- 'surface equivalent sphere diameter'
  D_surface = diameter of a sphere with the same surface as the particle
- 'Stokes equivalent sphere diameter'
  D_Stokes (= equivalent diameter corresponding to the diameter of a sphere with the same final settling velocity as the particle undergoing laminar flow in a fluid of the same density and viscosity)
- 'hydrodynamic equivalent sphere diameter'
  Hydrodynamic equivalent diameter D_hydro (= diameter of a sphere with the same translational diffusion coefficient as the particle in the same fluid under the same conditions)
  The diameter measured in Dynamic Light Scattering is called the hydrodynamic diameter and refers to the way a particle diffuses within a fluid. The diameter obtained by this technique is that of a sphere that has the same translational diffusion coefficient as the particle being measured.
  The translational diffusion coefficient will depend not only on the size of the particle 'core', but also on any surface structure, as well as the concentration and type of ions in the medium. This means that the size will be larger than measured by electron microscopy, for example, where the particle is removed from its native environment.
- 'sieve equivalent sphere diameter'
  D_sieve (= equivalent diameter corresponding to the diameter of a sphere passing through a sieve of defined mesh size with square or circular apertures).
- 'aerodynamic equivalent sphere diameter'
  The diameter in [nm] of an equivalent spherical particle with the same unit [1000 kg/m3] density and settling velocity in air as the NOAA under consideration. (ThinkWorks)
  The aerodynamic diameter of an irregular particle is defined as the diameter of the spherical particle with a density of 1000 kg/m3 and the same settling velocity as the irregular particle. (Wikipedia)
  The diameter of a sphere with unit density that has aerodynamic behavior identical to that of the particle in question; an expression of aerodynamic behavior of an irregularly shaped particle in terms of the diameter of an idealized particle. Particles having the same aerodynamic diameter may have different dimensions and shapes.
  [https://www.opentoxipedia.org/index.php/Aerodynamic_diameter]
  [constraint, only relevant if medium.physical_state = gas]
- 'volume equivalent cylinder diameter'
  diameter and length of a cylinder with the same volume as the fibre like particle.
- 'volume equivalent disc'
  thickness and diameter of a disc with the same volume as the disc/platelett like particle.

PSDWeighting

A particle size distribution can be represented in different ways with respect to the weighting of individual particles. The weighting mechanism will depend upon the measuring principle being used.
When comparing particle size data for the same sample measured by different techniques, it is important to realize that the types of distribution being measured and reported can produce very different particle size results.

- 'mass based'
  Here the contribution of each particle in the distribution relates to the mass of that particle (uniform density), i.e. the relative contribution will be proportional to (size)3. (check?)
  IUCLID PhraseID 9150 = mass based distribution
- 'number based'
  A counting technique such as image analysis will give a number weighted distribution where each particle is given equal weighting irrespective of its size.
  This is most often useful where knowing the absolute number of particles is important - in foreign particle detection for example - or where high resolution (particle by particle) is required.
  IUCLID PhraseID 1822 => counted distribution
- 'surface based'
- 'volume based'
  Here the contribution of each particle in the distribution relates to the volume of that particle (equivalent to mass if the density is uniform), i.e. the relative contribution will be proportional to (size)3.
  IUCLID PhraseID 2457 = volumetric distribution
- 'light intensity based'
  Dynamic light scattering techniques will give an intensity weighted distribution, where the contribution of each particle in the distribution relates to the intensity of light scattered by the particle. (unit ?)
  not in IUCLID

Dimension

The three dimensions of an object.

- D1
  D1 is the shortest of three dimensions (x,y,z)
- D2
  D2 the dimension considered either equal or between D1 and D3
- D3
  D3 is the longest of three dimensions (x,y,z)

OdourCategory

IULCID phrasegroup A100

- 'ammonia-like'
  IUCLID phrase 4759
- 'biting'
  1772
- 'characteristic of sulfur-containing compounds'
  3883
- 'characteristic of aromatic compounds'
  3884
- 'faint'
  4760
- 'garlic-like'
  3885
- 'odourless'
  2216
- 'pungent'
  2298
- 'slight'
  4761
- 'sweetish'
  2408
- 'other'

ShapeCategory
- scSpheroidal
- scElongated
- scPlatelets

ShapeSubCategory
- sscSpherical
- sscPyramidal
- ssCubic
- ssOrthorhombic
- sscPolyhedral
- sscTubes
- sscRods
- sscDiscs
- sscPlates

MaterialDataSource
- 'user defined'
- 'database'

DissolutionOutcome
- instantaneously
- quick
- gradual
- very_slow

DispersionOutcome
- stable
- intermediate
- unstable

ToxRatioOutcome
- high_ratio
- intermediate_ratio
- low_ratio

AffinityOutcome
- high_affinity
- low_affinity

AssemblyStructure

The assembly structure of the primary particle.
Good definitions required for these categories, also need to know if overlaps and/or combination are allowed..

- 'shell-like structures'
- 'multi-walled'
- 'nano-onions'
- 'multi-layers'
- 'hollow structures'

AssemblyStructure2nd
- 'individual fibres'
- 'aligned fibrous bundles'
- 'tangled fibrous bundles'
- 'granular agglomerate'

SpaceGroup

https://en.wikipedia.org/wiki/List_of_space_groups
+ 231 => Amorphous

- spg1
- spg2
- spg3
- spg4
- spg5
- spg6
- spg7
- spg8
- spg9
- spg10
- spg11
- spg12
- spg13
- spg14
- spg15
- spg16
- spg17
- spg18
- spg19
- spg20
- spg21
- spg22
- spg23
- spg24
- spg25
- spg26
- spg27
- spg28
- spg29
- spg30
- spg31
- spg32
- spg33
- spg34
- spg35
- spg36
- spg37

- spg38
- spg39
- spg40
- spg41
- spg42
- spg43
- spg44
- spg45
- spg46
- spg47
- spg48
- spg49
- spg50
- spg51
- spg52
- spg53
- spg54
- spg55
- spg56
- spg57
- spg58
- spg59
- spg60
- spg61
- spg62
- spg63
- spg64
- spg65
- spg66
- spg67
- spg68
- spg69
- spg70
- spg71
- spg72
- spg73
- spg74
- spg75
- spg76
- spg77
- spg78
- spg79
- spg80
- spg81
- spg82
- spg83
- spg84
- spg85
- spg86
- spg87
- spg88
- spg89
- spg90
- spg91
- spg92
- spg93
- spg94
- spg95
- spg96
- spg97
- spg98
- spg99
- spg100
- spg101
- spg102

- spg103
- spg104
- spg105
- spg106
- spg107
- spg108
- spg109
- spg110
- spg111
- spg112
- spg113
- spg114
- spg115
- spg116
- spg117
- spg118
- spg119
- spg120
- spg121
- spg122
- spg123
- spg124
- spg125
- spg126
- spg127
- spg128
- spg129
- spg130
- spg131
- spg132
- spg133
- spg134
- spg135
- spg136
- spg137
- spg138
- spg139
- spg140
- spg141
- spg142
- spg143
- spg144
- spg145
- spg146
- spg147
- spg148
- spg149
- spg150
- spg151
- spg152
- spg153
- spg154
- spg155
- spg156
- spg157
- spg158
- spg159
- spg160
- spg161
- spg162
- spg163
- spg164
- spg165
- spg166
- spg167

- spg168
- spg169
- spg170
- spg171
- spg172
- spg173
- spg174
- spg175
- spg176
- spg177
- spg178
- spg179
- spg180
- spg181
- spg182
- spg183
- spg184
- spg185
- spg186
- spg187
- spg188
- spg189
- spg190
- spg191
- spg192
- spg193
- spg194
- spg195
- spg196
- spg197
- spg198
- spg199
- spg200
- spg201
- spg202
- spg203
- spg204
- spg205
- spg206
- spg207
- spg208
- spg209
- spg210
- spg211
- spg212
- spg213
- spg214
- spg215
- spg216
- spg217
- spg218
- spg219
- spg220
- spg221
- spg222
- spg223
- spg224
- spg225
- spg226
- spg227
- spg228
- spg229
- spg230
- amorphous

SubstanceType

Substance type is used to organise substances or nanoforms according to their core composition and sometimes shape.

- CELLULOSE
- FULLERENES
  fullerenes[CHEBI_33128]
- NP_ALUMINIUM_OXIDE
  aluminium oxide nanoparticles, Al2O3 [ENM_9000005]
- NP_BARIUM_SULFATE
  BARIUM_SULFATE, BASO4 NM-220 [CHEBI_133326] the ontology entry doesn't refer to it as a nanoparticle but just a substance.
- NP_CARBON_BLACK
- NP_CERIUM_OXIDE
  cerium oxide nanoparticles [ENM_9000006]
- NP_DENDRIMERS
  dendrimers[NPO_735]
- NP_GOLD
  gold nanoparticles, AU [NPO_401]
- NP_IRON
  iron nanoparticles, Fe?? [ENM_9000200]
- NP_IRON_TRIOXIDE
- NP_MANGANESE_TRIOXIDE
- NP_MWCNT
  multi-walled carbon nanotubes [NPO_354]
- NP_NANOCLAY
  nanoclay nanoparticles [ENM_9000007]
- NP_SWCNT
  single-walled carbon nanotubes [NPO_943]
- NP_SILICON_DIOXIDE
  silicon dioxide nanoparticles, SiO2 [NPO_1373]
- NP_SILVER
  silver nanoparticles, Ag [NPO_1892]
- NP_TITANIUM_DIOXIDE
  titanium dioxide nanoparticles, TiO2 [CHEBI_51050]
- NP_ZINC_OXIDE
  zinc oxide nanoparticles, ZnO [NPO_1542]
- NP_FIBRILLAR_CELLULOSE

4.2 Defined classes

Class `Material` is kind of `EP_Owner`

Abstract material, representing substances, products, articles, mixtures.

Attributes

name	type	domain	inference	comment
name	: String			*Name of the material, substance, nanoform or chemical in order to identify it within the case.*
description	: String			*General description of the material, nanoform or chemical, to provide general information about it.*
constituent_role	:: ConstituentRole		Infer constituent role	*Identifies the role of this specific material in relationship to its composing material. (ThinkWorks) (see PhysicalState)* *Note! The role is not indicating its functional behaviour. It enables filtering and reasoning with specific constituents in any material.*
physical_state	:: PhysicalState		Infer physical state	*Indicates the physical state of the material. (ThinkWorks)*
surface_index	: Integer	# ≥ 0		*In case this material is a constituent the surface_index is used to indicate the relative position of it within the layout of the composing material. The surface_index is a relative value indicating the virtual layer this material is part of.* *The constituent(s) with the highest value are the most outward and considered the only chemicals to be in direct contact with the surrounding medium.*
category	:: CompositionCategory			*Indicates if the material is considered to be organic, inorganic or a combination. (completely defined by its constituents)*
functions	: MaterialFunctions			*Indicate which function(s) this material|constituent fulfils. (Important for Safer By Design.)*
s_uuid_hs	: String			*This is a unique substance identifier equal to the one in the eNanoMapper database. (when the material is constructed from the eNanoMapper database)*
colour	: String			
conc	: percentage	(# ≥ 0.0·%) and (# ≤ 100.0·%)	Infer conc	
data_source	:: MaterialDataSource			
density	: density_unit		Infer density	
viscosity	: Dynamic viscosity	# ≥ 0.0·mPa·s		
abrasive_wear_factor	: kilogram force			*Is this the correct unit? In IATA Oc-R-Indoor-2 => mm2/kgf (not verified)*
moisture_content	: percentage			
stype	:: SubstanceType			

Inference methods

Inference method: 'Infer physical state'

C1	ByUser(physical_state)	False			True
C2	PhysicalStateDomain(composer) | domain	0	1	ELSE	-
A1	physical_state	solid	domain[1]		
		R1	R2	R3	R4

Inference method: 'Infer constituent role'

C1	DP_FromProvided(EPQ(PC_COMPOSITION::EP_CONSTITUENT_ROLE)) | dp_role	nil							ELSE
C2	ByUser(constituent_role)	False				True			-
C3	ConstituentRoleDomain(composer) | domain	0	1	ELSE		0	ELSE		-
C4	Current(constituent_role) in domain	-	-	True	False	-	True	False	-
A1	constituent_role		domain[1]						dp_role.enum_y
A2	**Reset**(constituent_role)	X			X	X		X	
		R1	R2	R3	R4	R5	R6	R7	R8

Inference method: 'Infer conc'

C1	composer	nil	ELSE		
C2	DP_FromProvided(EPQU(PC_COMPOSITION::EP_MASS_CONC, %)) | dp_mass_perc	-	nil	ELSE	
C3	ByUser(conc)	-	True	False	-
A1	conc	100%			dp_mass_perc.value_y

A2	**with** composer.constituents→Reject(c | ByUser(c.conc))→Size | nr **do**
	begin
	  if nr = 1 **then**
	  conc != ConcentrationDomainMax() **as** %
	  else
	  conc != 0.0%
	end
				X	

		R1	R2	R3	R4

Inference method: 'Infer density'

C1	DP_From(EPQU(PC_DENSITY::EP_SKELETAL_DENSITY, density_unit)) | dp	nil	ELSE
A1	density		dp.value_y as density_unit
		R1	R2

Inference method: ''

C1	DP_FromProvided(EPQ(PC_COMPOSITION::EP_COMPOSITION_CATEGORY)) | dp_cat	nil	ELSE
A1	category		dp_cat.enum_y
A2	**Reset**(category)	X	
		R1	R2

Defined expressions

name	type	expression	comment
chemistry	: Chemicals	constituents.chemistry→Sum	*All chemicals defined within this material. (the leaves of the constituent tree)*
surface_chemistry	: Chemicals	Chemicals{}	*All chemicals defined within this material directly in contact with the surrounding (external) medium. (based on highest surface_index)*
core_chemistry	: Chemicals	chemistry→Select(ch | ch.constituent_ role **in** ConstituentRole{'core', 'wall', 'main chemical'})	*All chemicals defined within this material with a surface_index equal or lower to the [core, wall, capsule] chemicals with the lowest surface_index.*
is_particulate	: Boolean	False	*True if, the material is free to move within the composing material or surrounding medium.*
type_category	: String	"material"	
name_path	: String	composer→**If**(c | c.name_path + " | " + **name**, **name**)	*The name with the preceeding path of composer names.*
all_constituents	: Materials	constituents.all_constituents→Sum→Prepend(self)	
scenario	: Scenario	composer→**If**(c | c.scenario, \)	*composer*
is_eNanoMapper_substance	: Boolean	ByUser(s_uuid_hs) **and** (s_uuid_hs ≠ "")	
v_self	: Material	self	*This is the virtual self. It's always the self of the material object itself except in case of a proxy material object, then it results in the self of the original material the proxy is representing.*
nano_constituents	: Nanoforms	all_constituents→ElementsOf(Nanoform)	*All nanoforms contained within this material.*
nano_enabled	: Boolean	nano_constituents→NotEmpty	
abbreviation	: String	"MATR"	
hcodes	: HCodes	HCodes()	
dissolved_name	: String	**name** + "invalid"	
candidate_NFs	: Nanoforms	Nanoforms{}	*The candidate nanoform this material represents.Only Nanoform and CandidateNFProxy can represent one or more nano-forms.*

Operators

```
function Material.CategoryEndpointDomain(): Enumerations [specialization]
|  Relevant_CategoryEndpoints()
```

```
function Material.DP_From( epq : EP_Qualifier ): EP_DataObject [specialization]
  begin
    /* Find qualified assay endpoint records  */  ;
    with DP_FromAssays(epq) | assays_dp then
    begin
      result := assays_dp
    end;
    /* Find decision node derived endpoint records */  ;
    if result = nil then
      with DP_FromProvided(epq) | estimate_dp then
      begin
        result := estimate_dp
      end
  end
```

function Material.Relevant_CategoryEndpoints(): Enumerations

C1		-
A1	/* Classification and labelling endpoints */	
A2	result→Add(PC_CLASSIFICATION_LABELING)	X
A3	/* Physicochemical category endpoints*/	
A4	result→Add(PC_COMPOSITION)	X
A5	result→Add(PC_APPEARANCE)	X
A6	result→Add(PC_MELTING)	X
A7	result→Add(PC_BOILING)	X
A8	result→Add(PC_DENSITY)	X
A9	result→Add(PC_GRANULOMETRY)	X
A10	result→Add(PC_VAPOUR)	X
A11	result→Add(PC_PARTITION)	
A12	result→Add(PC_WATER_SOL)	X
A13	result→Add(PC_SOL_ORGANIC)	
A14	result→Add(PC_SURFACE_TENSION)	X
A15	result→Add(PC_STABILITY_THERMAL_SUNLIGHT_METALS)	X
A16	result→Add(PC_NON_SATURATED_PH)	X
A17	result→Add(PC_DISSOCIATION)	
A18	result→Add(PC_VISCOSITY)	X
A19	/* Nanomaterial specific category endpoints */	
A20	result→Add(PC_AGGLOMERATION_AGGREGATION)	X
A21	result→Add(PC_CRYSTALLINE_PHASE)	X
A22	result→Add(PC_CRYSTALLITE_AND_GRAIN_SIZE)	X
A23	result→Add(PC_ASPECT_RATIO_SHAPE)	X
A24	result→Add(PC_SPECIFIC_SURFACE_AREA)	X
A25	result→Add(PC_ZETA_POTENTIAL)	X
A26	result→Add(PC_SURFACE_CHEMISTRY)	X
A27	result→Add(PC_AEROSOL_CHARACTERISATION)	X
A28	result→Add(PC_DUSTINESS)	X
A29	result→Add(PC_POROSITY)	X
A30	result→Add(PC_POUR_DENSITY)	X
A31	result→Add(PC_PHOTOCATALYTIC_ACTIVITY)	X
A32	result→Add(PC_RADICAL_FORMATION_POTENTIAL)	X
A33	result→Add(PC_CATALYTIC_ACTIVITY)	X
A34	result→Add(PC_RIGIDITY)	X
A35	result→Add(PC_BIOMOL_INTERACTION)	X
A36	/* Environmental fate and behaviour */	
A37	result→Add(EN_PHOTOTRANS_AIR)	X
A38	result→Add(EN_HYDROLYSIS)	X
A39	result→Add(EN_PHOTOTRANS_WATER)	X
A40	result→Add(EN_PHOTOTRANS_SOIL)	X

A41	result→Add(EN_BIODEG_WATER_SCREEN)	X
A42	result→Add(EN_BIODEG_WATER_SIM)	X
A43	result→Add(EN_BIODEG_SOIL)	X
A44	result→Add(EN_DEGR_MODE_IN_USE)	X
A45	result→Add(EN_BIOACCU_AQUATIC_SED)	X
A46	result→Add(EN_BIOACCU_TERRESTRIAL)	X
A47	result→Add(EN_ADSORPTION)	X
A48	result→Add(EN_HENRY_LAW)	X
A49	result→Add(EN_DISPERSION_STABILITY_NANOMATERIAL)	X
A50	/* Effects on biotic systems */	
A51	result→Add(EC_FISH_TOX_SHORT)	X
A52	result→Add(EC_FISH_TOX_CHRONIC)	X
A53	result→Add(EC_AQUATIC_INVERT_TOX_SHORT)	X
A54	result→Add(EC_AQUATIC_INVERT_TOX_CHRONIC)	X
A55	result→Add(EC_ALGAE_TOX)	X
A56	result→Add(EC_AQ_PLANTS_NONE_ALGAE)	X
A57	result→Add(EC_BAC_TOX)	X
A58	result→Add(EC_SEDIMENT_TOX)	X
A59	result→Add(EC_SOIL_TOX)	X
A60	result→Add(EC_TERR_ARTHROP_TOX)	X
A61	result→Add(EC_TERR_PLANT_TOX)	X
A62	result→Add(EC_SOIL_MICRO_TOX)	X
A63	result→Add(EC_BIRDS_TOX)	X
A64	/* Health effects */	
A65	result→Add(HH_BASIC_TOX)	X
A66	result→Add(HH_DERMAL_ABSORP)	X
A67	result→Add(HH_ACUTE_TOX_ORAL)	X
A68	result→Add(HH_ACUTE_TOX_INHAL)	X
A69	result→Add(HH_ACUTE_TOX_DERMAL)	X
A70	result→Add(HH_SKIN_IRRITATION)	X
A71	result→Add(HH_EYE_IRRITATION)	X
A72	result→Add(HH_SKIN_SENSITISATION)	X
A73	result→Add(HH_RESP_SENSITISATION)	X
A74	result→Add(HH_REPEATED_ORAL)	X
A75	result→Add(HH_REPEATED_INHAL)	X
A76	result→Add(HH_REPEATED_DERMAL)	X
A77	result→Add(HH_GENETIC_IN_VITRO)	X
A78	result→Add(HH_GENETIC_IN_VIVO)	X
A79	result→Add(HH_LUNG_INSTILLATION)	X
A80	result→Add(HH_CYTOTOXICITY)	X
A81	result→Add(HH_INFLAMMATION)	X

A82	result→Add(HH_FIBROSIS)	X
A83	result→Add(HH_OXIDATIVE_STRESS)	X
A84	result→Add(HH_CELLULAR_INTERNALIZATION)	X
A85	result→Add(HH_CARCINOGENICITY)	X
A86	result→Add(HH_REPRODUCTION)	X
A87	result→Add(HH_DEVELOPMENTAL)	X
A88	result→Add(HH_NEUROTOXICITY)	X
A89	result→Add(HH_IMMUNOTOXICITY)	X
A90	result→Add(HH_BARRIER_INTEGRITY)	X
A91	result→Add(HH_LUNG_DEPOSITION)	X
A92	/* Use, Release Exposure */	
A93	result→Add(UE_MANUFACTURE)	X
A94	result→Add(UE_FORMULATING_REPACKING)	X
A95	result→Add(UE_USES_AT_INDUSTRIAL_SITES)	X
A96	result→Add(UE_WIDESPREAD_USE_WORKERS)	X
A97	result→Add(UE_CONSUMER_**USES**)	X
A98	result→Add(UE_SERVICE_LIFE)	X
		R1

```
function Material.Relevant_AssayClasses(): AssayClasses
  with Relevant_CategoryEndpoints() | category_endpoints then
    result := Assay→Leaves→AsSequence→Select(assay | (category_endpoints * assay.ResultEndpointDomain()→Collect(ep | ep→Enumeration))→NotEmpty)

constructor Material.Create()
|  self→New

function Material.Add_Constituent(material_class :: Material ): Material
  if material_class ≠ nil then
    with material_class.Create() | newMaterial then
    begin
      result := newMaterial;
      self→AddComponent(constituents, newMaterial);
      newMaterial.Initialize()
    end

function Material.ConstituentRoleDomain(composing_context : Material ): ConstituentRoles
|  ConstituentRoles{}
```

```
function Material.RoleCombinationsDomain(constituent : Material,constituent_domain : ConstituentRoles ): ConstituentRoles
  with constituents→Reject(c | (c.v_self = constituent) or (Current(c.constituent_role) = nil)) | other_constituents do
    with other_constituents→Collect(oc | Current(oc.constituent_role)) | other_roles do
    begin
      if other_constituents→Exists(c | ByUser(c.constituent_role) and (Current(c.constituent_role) = 'mixed')) then
      begin
        /* This substance already has a mixed solid, only other mixed solids are still allowed. */      ;
        result := (constituent_domain * ConstituentRoles{'mixed'})→AsSequence
      end
      else
        if other_constituents→Exists(c | ByUser(c.constituent_role) and (Current(c.constituent_role) = 'layered')) then
        begin
          /* This substance already has a layered solid, only other layered solids are still allowed. */        ;
          result := (constituent_domain * ConstituentRoles{'layered'})→AsSequence
        end
        else
          if other_constituents→Exists(c | ByUser(c.constituent_role) and (Current(c.constituent_role) = 'capsule')) then
          begin
            /* This substance has a mrCapsule */          ;
            result := (constituent_domain * ConstituentRoles{'encapsulated'})→AsSequence
          end
          else
            if 'solid matrix' in other_roles then
            begin
              /* This substance already has a solid matrix defined. Remove the other continuous media and also mixed and layered. */            ;
              result := constituent_domain - ConstituentRoles{'solid matrix', 'liquid medium', 'gaseous medium', 'mixed', 'layered'}
            end
            else
              if 'liquid medium' in other_roles then
              begin
                /* This substance already has a liquid medium defined. Remove the other continuous media and also mixed and layered */              ;
                result := constituent_domain - ConstituentRoles{'solid matrix', 'liquid medium', 'gaseous medium', 'mixed', 'layered'};
                /* No solid matrix, so remove surface bound, film etc */              ;
                result := result - ConstituentRoles{'surface bound', 'film'}
              end
              else
              if 'gaseous medium' in other_roles then
              begin
                /* This substance already has a gaseous medium defined. Remove the other none gaseous media and possible dissolved role. */                ;
                result := constituent_domain - ConstituentRoles{'solid matrix', 'liquid medium', 'dissolved', 'mixed', 'layered'};
                /* No solid matrix, so remove surface bound, film etc */              ;
                result := result - ConstituentRoles{'surface bound', 'film'}
              end
              else
              begin
                /* No continuous medium defined yet */              ;
                case constituent.physical_state of
                  solid:
                    result := (constituent_domain * ConstituentRoles{'solid matrix', 'substrate', 'mixed', 'layered', 'capsule'})→AsSequence;
                  liquid:
                    result := (constituent_domain * ConstituentRoles{'liquid medium', 'film'})→AsSequence;
                  gas:
                    result := (constituent_domain * ConstituentRoles{'gaseous medium'})→AsSequence
                  else
                    result := ConstituentRoles{}
                end
              end
end
```

function Material.PhysicalStateDomain(composing_context : Material): PhysicalStates

C1	constituents	0	1	ELSE
A1	result	PhysicalStates{solid, liquid, gas}		
A2	result→Add(#)		constituents[1].physical_state	

A3	**with** GetSubstanceCategories()→Collect(mc | DeriveStateFromSubstanceCategory(mc))→Unique | states **then**
	begin
	  if states→Size = 1 **then**
	  if states[1] ≠ **nil then**
	  result := PhysicalStates{states[1]}
	  else
	  result := PhysicalStates{'mixed state'}
	end
				X

		R1	R2	R3

```
function Material.GetSubstanceCategories(): SubstanceCategories
  if constituents→Size > 1 then
  begin
    /* First we have to find the continous media, only one continuous medium may exist at the same time. */  ;
    with constituents→Any(c | Current(c.constituent_role) in ConstituentRole{'solid matrix', 'substrate', 'liquid medium', 'gaseous medium'}) | continuous_medium then
    begin
      /* Find constituents either dissolved or dispersed in the continuous medium */    ;
      with constituents→Select(c | Current(c.constituent_role) in ConstituentRole{'dissolved', 'dispersed'}) | disp_constituents then
      begin
        foreach dc of disp_constituents do
        begin
          with dc.DerivePhaseSizes() | phase_sizes then
          begin
            foreach ps of phase_sizes do
              with DeriveMixtureCategory(dc.physical_state, continuous_medium.physical_state, ps) | mc then
                result→Add(mc)
          end
          else
          begin
            with DeriveMixtureCategory(dc.physical_state, continuous_medium.physical_state, nil) | mc then
              result→Add(mc)
          end
        end
      end;
      /* Find constituents attached/bound to the surface of a solid continuous medium */    ;
      if Current(continuous_medium.constituent_role) in ConstituentRole{'solid matrix', 'substrate'} then
      begin
        with constituents→Select(c | Current(c.constituent_role) in ConstituentRole{'surface bound', 'film'}) | surface_constituents then
        begin
          foreach sc of surface_constituents do
          begin
            result→Add('composite')
          end
        end
      end
      else
        if constituents→ForAll(c | Current(c.constituent_role) in ConstituentRole{'mixed'}) then
        begin
          /* As there are no continuous media defined, we may have solid constituents mixed together, like gravel */      ;
          result→Add('solid mixture')
        end
        else
          if constituents→ForAll(c | Current(c.constituent_role) in ConstituentRole{'layered'}) then
          begin
            /* As there are no continuous media defined, we may have layered solid constituents, like laminate */        ;
            result→Add('composite')
          end
          else
            if constituents→Exists(c | Current(c.constituent_role) in ConstituentRole{'capsule'}) then
            begin
              /* As there are no continuous media defined, we may have capsules */          ;
              with constituents→Collect(c | Current(c.constituent_role)) - ConstituentRole{'capsule'} | other_roles then
                if other_roles→ForAll(r | r = 'encapsulated') then
                  result→Add(SubstanceCategory::'capsule')
            end
            else
              result := SubstanceCategories{'none'}  ;
    result := result→Unique
  end
  else
  begin
    /* No or a single constituent found */  ;
    result := SubstanceCategories{'none'}
  end

function Material.DerivePhaseSizes(): PhaseSizes
|  PhaseSizes{continuous}
```

```
function Material.ConcentrationDomainMax(): percentage
  if composer ≠ nil then
  begin
    with composer.constituents→Excluding(self)→Select(c | ByUser(c.conc)).conc→Sum | percentage_set do
    begin
      with (100.0·% - percentage_set)→Max(0.0·%) | percentage_left do
      begin
        result := percentage_left
      end
    end
  end
  else
  begin
  end

function Material.HCodes(): HCodes
  begin
    foreach hs of hazard_statements do
    begin
      if hs.hcode ≠ nil then
      begin
        if conc ≥ hs.specific_concentration_limit then
          result→Add(hs.hcode)
      end
    end;
    result := result + constituents.HCodes()→Sum→Unique
  end

function Material.CompositionCategoryDomain(): CompositionCategories
| CompositionCategories{}

function Material.DP_FromAssays(epq : EP_Qualifier ): EP_DataObject
  begin
    result := Datapoint_FromAssays(assays, epq);
    if result = nil then
      with Convertors(epq) | convertors then
      begin
        with convertors[1] | convertor do
          with convertor.SourceQualifier(epq) | src_epq then
          begin
            with Datapoint_FromAssays(assays, src_epq) | src_dp then
            begin
              with convertor.Convert_DP(src_epq, src_dp, epq) | dp then
              begin
                result := dp
              end
            end
          end
      end
  end
```

Defined composites

Any instance of `Material` is composed of

- zero or more `constituents` of any kind of Material *General, any material (composer) must define its constituents (any material) up to the level of the individual chemicals. There are constraints on the multiplicity and potential constituents per material class. A 'chemical' may not have any constituents, any other material must have at least one constituent.*
- zero or more `assays` of any kind of Assay
- zero or more `hazard_statements` of CLP_Hazard

Class `Substance` is kind of `Material`

A substance is defined in REACH by Article 3 and in CLP by Article 2 as:

'a chemical element and its compounds in the natural state or obtained by any manufacturing process,
including any additive necessary to preserve its stability and any impurity deriving from the process used,
but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.'

REACH encompasses substances (mono-constituent, multi-constituent, UVCB substances and 'nanoform' (new!)) which all should be addressed as substances.

Defined expressions

name	type	expression	comment
abbreviation	: String	"SUBST"	

Operators

```
function Substance.CompositionCategoryDomain(): CompositionCategories [specialization]
|  CompositionCategories{'organic compound', 'inorganic compound', 'water'}
```

Class `Nanoform` is kind of `Substance`

Represents an individual nanoform.

A "nanoform" is a form of a natural or 20 manufactured substance consisting of particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm, including also by derogation fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm.

Attributes

name	type	domain	inference	comment
nm_code	: String			
is_HARN	:: YesNo		Infer, is HARN	*To be considered a HARN at the Basic Information step of the Framework requires only that the NF has an elongated structure with an aspect ratio > 5:1 (European Chemicals Agency, 2019).*
DN_HARN_can_deposit_in_distal_region_of_lung	:: YesNo		TTS, HARN can deposit in the distil lung	*In order to address this DN evidence that the NF has an aerodynamic diameter (Dae) of < 4 µm is required as this represents the respirable portion of inhalable particles that enter the non-ciliated alveoli (d50 = 4 µm) (BSI, 1993)*
DN_HARN_can_deposit_in_distal_region_of_lung_TL	:: TierLevel			
DN_HARNs_dissolve_very_slow_in_lung_lining_fluid	:: YesNo		TTS, HARNs dissolve very slowly in lung lining fluid	*The half-life (t½ > 60 days) and dissolution rate (Kdiss < 1 ng/cm2/h) thresholds were set to ensure only very slowly dissolving HARNs meet the DN criteria. These thresholds are based on literature from durability and biopersistence studies of mineral fibres and also recent studies of metal oxide NFs; less than 1 % dissolution after 56 days in phagolysosomal fluid has been reported for biopersistent crocidolite asbestos, whereas non-biopersistent MMVF22 showed 50 % dissolution in the same timeframe (Maxim et al., 2002). Biopersistent fibres or very slowly dissolving NFs should be used as benchmark materials for inclusion in acellular assays to confirm DN outcomes for grouping target NFs as very slowing dissolving HARNs.*
DN_HARNs_dissolve_very_slow_in_lung_lining_fluid_TL	:: TierLevel			
DN_HARNs_dissolve_very_slow_in_lysosomal_fluid	:: YesNo		TTS, HARNs dissolve very slowly in lysosomal fluid	
DN_HARNs_dissolve_very_slow_in_lysosomal_fluid_TL	:: TierLevel			
DN_HARN_length_exceeds_5_micron	:: YesNo			
DN_HARN_length_exceeds_5_micron_TL	:: TierLevel			
DN_HARNs_are_rigid_and_needle_like	:: YesNo		TTS, is HARN rigid and maintain a fibrous, needle like morphology	
DN_HARNs_are_rigid_and_needle_like_TL	:: TierLevel			
DN_HARNs_cause_frustrated_phagocytosis	:: YesNo			
DN_HARNs_cause_frustrated_phagocytosis_TL	:: TierLevel			
DG_HARN_inflammation_TL	:: TierLevel			
DG_HARN_genotoxicity_TL	:: TierLevel			
DN_dissolution_in_lung_lining_fluid_TL	:: TierLevel			
DN_dissolution_outcome_in_lung_lining_fluid	:: DissolutionOutcome	DissolutionOutcome{instantaneously, quick, gradual, very_slow}	TTS, dissolution outcome in lung lining fluid	*Dissolution rate thresholds to be revised!! TO DO VNR* *$k > 1 \cdot ng \cdot cm^{-2} \cdot h^{-1}$ => half life 60 days above is considere slow* *1 ng/cm2/h we had should be equivalent to aroudn 60 d for a 50 m2/g SSA particle* *8300 ng/cm2/h => 10 min for a 50m2/g SSA particle*
DN_dissolution_in_lysosomal_fluid_TL	:: TierLevel			
DN_dissolution_outcome_in_lysosomal_fluid	:: DissolutionOutcome	DissolutionOutcome{instantaneously, quick, gradual, very_slow}	TTS, dissolution outcome in lysosomal fluid	
DN_dissolution_in_GI_fluids_TL	:: TierLevel			
DN_dissolution_outcome_in_GI_fluids	:: DissolutionOutcome	DissolutionOutcome{instantaneously, quick, gradual, very_slow}	TTS, dissolution outcome in GI fluids	
DN_dissolution_in_sweat_fluid_TL	:: TierLevel			
DN_dissolution_outcome_in_sweat_fluid	:: DissolutionOutcome		TTS, dissolution outcome in sweat fluid	

DG_reactivity_TL	:: TierLevel				
DG_inflammation_TL	:: TierLevel				
DG_reactivity_intestinal_TL	:: TierLevel				
DG_reactivity_bacterial_TL	:: TierLevel				
DG_reactivity_secondary_organs_TL	:: TierLevel				
DG_cytotoxicity_intestinal_TL	:: TierLevel				
DG_cytotoxicity_bacterial_TL	:: TierLevel				
DG_cytoxocity_secondary_organs_TL	:: TierLevel				
DG_barrier_integrity_intestinal_TL	:: TierLevel				
DG_barrier_integrity_bacterial_TL	:: TierLevel				
DG_inflammation_intestinal_TL	:: TierLevel				
DG_inflammation_secondary_organs_TL	:: TierLevel				
DG_genotoxicity_intestinal_TL	:: TierLevel				
DG_genotoxicity_secondary_organs_TL	:: TierLevel				
DN_is_inorganic_or_non_flexible_organic	:: YesNo				
DN_constituent_particle_diameter_exceeds_5nm	:: YesNo				
DN_NF_contains_or_degrades_to_CLP_classified_substances	:: YesNo				*DN_NF_contains_or_degrades_to_CLP_classified_substances*
DN_classified_substances_content_above_thresholds_for_classification_of_mixtures	:: YesNo				
DN_dissolution_outcome_in_fish_gut_saline	:: DissolutionOutcome		TTS, dissolution outcome in gut saline fluid		
DN_dissolution_in_fish_gut_saline_TL	:: TierLevel				
DN_dissolved_fraction_classified_substances_in_sweat_fluid_above_thresholds_for_classification_of_mixtures	:: YesNo				

Inference methods

Inference method: 'Infer, physical state'

C1	ByUser(physical_state)	False	True
A1	physical_state	solid	
		R1	R2

Inference method: 'Infer, is HARN'

C1	dp_aspect_ratio_D3_D1	nil	ELSE			
C2	dp_aspect_ratio_D3_D1.value_y | ar	-	ar > 5			ELSE
C3	DP_From(ENUM(EPQ(EP_SHAPE_CATEGORY), scElongated)) | dp	-	nil	ELSE		-
C4	dp.value_y > 0.0·%	-	-	True	False	-
A1	is_HARN			Yes	No	No
A2	**Reset**(is_HARN)	X	X			
		R1	R2	R3	R4	R5

Inference method: 'TTS, HARN can deposit in the distil lung'

C1	DN_HARN_can_deposit_in_distal_region_of_lung_TL	TL1				TL2				TL3	
C2	DP_From(EPQU(PC_GRANULOMETRY::EP_AERODYNAMIC_EQ_SPHERE_DIAMETER, ·µm)) | dp_Dea	nil		dp_Dea.value_y < 4.0·µm	ELSE	-				-	
C3	DP_From(MEAS(EPQU(PC_GRANULOMETRY::EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER, ·µm))) | dp_MDDA	-		-	-	nil		dp_MDDA.value_y < 4.0·µm	ELSE	-	
C4	ByUser(DN_HARN_can_deposit_in_distal_region_of_lung)	False	True	-	-	False	True	-	-	False	True
A1	DN_HARN_can_deposit_in_distal_region_of_lung			Yes	No			Yes			
A2	**Reset**(DN_HARN_can_deposit_in_distal_region_of_lung)	X				X				X	
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

Inference method: 'TTS, HARNs dissolve very slowly in lung lining fluid'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, ·%), 'Simulated lung airway lining fluid')) | dp_mass_loss	nil					ELSE		
C2	dp_mass_loss.value_y | mass_loss	-					mass_loss < 10.0·%	ELSE	
C3	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated lung airway lining fluid')) | dp_halftime	nil			ELSE		-	-	
C4	dp_halftime.value_y | ht	-			ht > 60.0·d	ELSE	-	-	
C5	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_RATE, dissolution_rate_unit), 'Simulated lung airway lining fluid')) | dp_rate	nil	ELSE		-	-	-	-	
C6	dp_rate.value_y | r	-	r < 1.0·ng·cm⁻²·h⁻¹	ELSE	-	-	-	-	
C7	ByUser(DN_HARNs_dissolve_very_slow_in_lung_lining_fluid)	-	-	-	-	-	-	True	False
A1	DN_HARNs_dissolve_very_slow_in_lung_lining_fluid		Yes	No	Yes	No	Yes		
A2	**Reset**(DN_HARNs_dissolve_very_slow_in_lung_lining_fluid)								X
		R1	R2	R3	R4	R5	R6	R7	R8

Inference method: 'TTS, dissolution outcome in lung lining fluid'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated lung airway lining fluid')) | dp_halftime	nil						ELSE		
C2	dp_halftime.value_y | ht	-						ht > 60.0·d	ht ≥ 48.0·h	ht ≥ 10.0·min	ELSE
C3	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_RATE, dissolution_rate_unit), 'Simulated lung airway lining fluid')) | dp_rate	nil		ELSE				-	-	-	-
C4	dp_rate.value_y | k	-		k > 8300.0·ng·cm⁻²·h⁻¹	k ≥ 100.0·ng·cm⁻²·h⁻¹	k ≥ 1.0·ng·cm⁻²·h⁻¹	ELSE	-	-	-	-
C5	ByUser(DN_dissolution_outcome_in_lung_lining_fluid)	False	True	-	-	-	-	-	-	-	-
A1	DN_dissolution_outcome_in_lung_lining_fluid			instantaneously	quick	gradual	very_slow	very_slow	gradual	quick	instantaneously
A2	**Reset**(DN_dissolution_outcome_in_lung_lining_fluid)	X									
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

Inference method: 'TTS, dissolution outcome in lysosomal fluid'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated lung macrophage phagolysosomal fluid')) | dp_halftime	nil					ELSE		
C2	dp_halftime.value_y | ht	-					ht > 60.0·d	ht > 48.0·h	ELSE
C3	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_RATE, dissolution_rate_unit), 'Simulated lung macrophage phagolysosomal fluid')) | dp_rate	nil		ELSE			-	-	-
C4	dp_rate.value_y | k	-		k > 100.0·ng·cm⁻²·h⁻¹	k ≥ 1.0·ng·cm⁻²·h⁻¹	ELSE	-	-	-
C5	ByUser(DN_dissolution_outcome_in_lysosomal_fluid)	True	False	-	-	-	-	-	-
A1	DN_dissolution_outcome_in_lysosomal_fluid			quick	gradual	very_slow	very_slow	gradual	quick
A2	**Reset**(DN_dissolution_outcome_in_lysosomal_fluid)		X						
		R1	R2	R3	R4	R5	R6	R7	R8

Inference method: 'TTS, dissolution outcome in GI fluids'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated saliva (5min) + gastric(2h) + intestinal fluid')) | dp_halftime	nil		ELSE			
C2	dp_halftime.value_y | ht	-		ht > 60.0·h	ht > 2.0·h	ht > 10.0·min	ELSE
C3	ByUser(DN_dissolution_outcome_in_GI_fluids)	True	False	-	-	-	-
A1	DN_dissolution_outcome_in_GI_fluids			very_slow	gradual	quick	instantaneously
A2	**Reset**(DN_dissolution_outcome_in_GI_fluids)		X				
		R1	R2	R3	R4	R5	R6

Inference method: 'TTS, dissolution outcome in sweat fluid'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated sweat')) | dp_halftime	nil		ELSE	
C2	dp_halftime.value_y | ht	-		ht ≥ 1.0·h	ELSE
C3	ByUser(DN_dissolution_outcome_in_sweat_fluid)	True	False	-	-
A1	DN_dissolution_outcome_in_sweat_fluid			gradual	instantaneously
A2	**Reset**(DN_dissolution_outcome_in_sweat_fluid)		X		
		R1	R2	R3	R4

Inference method: 'TTS, HARNs dissolve very slowly in lysosomal fluid'

C1	DN_HARNs_dissolve_very_slow_in_lysosomal_fluid_TL	TL3			TL2							TL1															
C2	DP_From(EPQU(MH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_TIME, ·d)) | dp_ivv_half_time	nil		ELSE	nil						ELSE	nil															
C3	dp_ivv_half_time.value_y > 60.0·d	-		True	False	-					True	False	-											True	False		
C4	DP_From(MED(EPQU(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_MASS_LOSS, ·%), 'Cell culture medium, pH 7.4')) | dp_mass_loss2	-		-	nil					ELSE		-	-	nil								ELSE			-	-	
C5	dp_mass_loss2.value_y < 10.0·%	-		-	-					True	False	-	-	-								True	False		-	-	
C6	DP_From(MED(EPQU(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_HALF_TIME, ·d), 'Cell culture medium, pH 7.4')) | dp_half_time2	-		-	nil				ELSE		-	-	-	-	nil							ELSE		-	-	-	-
C7	dp_half_time2.value_y > 60.0·d	-		-	-				True	False	-	-	-	-	-							True	False	-	-	-	-
C8	DP_From(MED(EPQU(PC_WATER_SOL::EP_INTRACELLULAR_DISSOLUTION_RATE, ·d), 'Cell culture medium, pH 7.4')) | dp_rate2	-		-	nil		ELSE		-	-	-	-	-	-	nil						ELSE		-	-	-	-	-
C9	dp_rate2.value_y < 1.0·ng·cm⁻²·h⁻¹	-		-	-		True	False	-	-	-	-	-	-	-					True	False	-	-	-	-	-	-
C10	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_MASS_LOSS, ·%), 'Simulated lung macrophage phagolysosomal fluid')) | dp_mass_loss	-		-	-		-	-	-	-	-	-	-	-	nil				ELSE		-	-	-	-	-	-	-
C11	dp_mass_loss.value_y < 10.0·%	-		-	-		-	-	-	-	-	-	-	-	-				True	False	-	-	-	-	-	-	-
C12	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Simulated lung macrophage phagolysosomal fluid')) | dp_half_time	-		-	-		-	-	-	-	-	-	-	-	nil		ELSE		-	-	-	-	-	-	-	-	-
C13	dp_half_time.value_y > 60.0·d	-		-	-		-	-	-	-	-	-	-	-	-		True	False	-	-	-	-	-	-	-	-	-
C14	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_RATE, dissolution_rate_unit), 'Simulated lung macrophage phagolysosomal fluid')) | dp_rate	-		-	-		-	-	-	-	-	-	-	nil		ELSE		-	-	-	-	-	-	-	-	-	-
C15	dp_rate.value_y < 1.0·ng·cm⁻²·h⁻¹	-		-	-		-	-	-	-	-	-	-	-		True	False	-	-	-	-	-	-	-	-	-	-
C16	ByUser(DN_HARNs_dissolve_very_slow_in_lysosomal_fluid)	True	False	-	-	True	False	-	-	-	-	-	-	True	False	-	-	-	-	-	-	-	-	-	-	-	-
A1	DN_HARNs_dissolve_very_slow_in_lysosomal_fluid			Yes	No			Yes	No	Yes	No	Yes	No	Yes	No			Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
A2	**Reset**(DN_HARNs_dissolve_very_slow_in_lysosomal_fluid)		X				X								X												
A3	DN_HARNs_dissolve_very_slow_in_lysosomal_fluid_TL													TL3	TL3							TL2	TL2	TL2	TL2	TL2	TL2	TL3	TL3
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24	R25	R26	R27	R28	R29	R30

Inference method: 'TTS, is HARN rigid and maintain a fibrous, needle like morphology'

C1	DN_HARNs_are_rigid_and_needle_like_TL | tl	TL1, TL2																										ELSE
C2	(tl = TL1)→If('Sterile filtered water', 'Aerolisation medium') | medium	nil	ELSE																									-
C3	DP_From(MED(EPQ(EP_ASSEMBLY_STRUCTURE_AGG), medium)) | dp_as_2nd	-	nil	ELSE																								-
C4	dp_as_2nd.enum_y	-	-	'individual fibres'			'aligned fibrous bundles'									'tangled fibrous bundles'						'granular agglomerate'					ELSE	-
C5	DP_From(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slConstituentParticleLevel), medium)) | dp_D50_D1_1st	-	-	nil	ELSE		-									-						-					-	-
C6	dp_D50_D1_1st.value_y as ·nm | d_l1	-	-	-	d_l1 < 30.0·nm	ELSE	-									-						-					-	-
C7	DP_From(MED(ENUM(EPQ(EP_ASPECT_RATIO_D3_D1), slAgglomerateLevel), medium)) | dp_AR_2nd	-	-	-	-	-	nil	ELSE								nil	ELSE					nil	ELSE				-	-
C8	dp_AR_2nd.value_y | AR_2nd	-	-	-	-	-	-	AR_2nd > 3					ELSE			-	AR_2nd < 3		ELSE			-	AR_2nd < 3		ELSE		-	-
C9	DP_From(MED(ENUM(PER(EPQ(EP_DnPx_D1), 50.0·%), slAgglomerateLevel), medium)) | dp_D50_D1_2nd	-	-	-	-	-	-	nil	ELSE							-	-	-	-			-	-	-	-		-	-
C10	dp_D50_D1_2nd.value_y as ·nm | d_l2	-	-	-	-	-	-	-	d_l2 > 30.0·nm			ELSE				-	-	-	-			-	-	-	-		-	-
A1	DN_HARNs_are_rigid_and_needle_like				No	Yes			Yes								Yes						No						
A2	**if not** ByUser(DN_HARNs_are_rigid_and_needle_like) **then** **Reset**(DN_HARNs_are_rigid_and_needle_like)	X	X	X			X	X			X	X	X			X	X			X	X			X	X	X	X	X
		R1	R2	R3	R4	R5	R6	R7	R8		R9	R10	R11	R12		R13	R14	R15		R16	R17	R18	R19	R20	R21	R22	R23	R24	R25	R26	R27	R28	R29	R30	R18

Inference method: 'TTS, dissolution outcome in gut saline fluid'

C1	DP_From(MED(EPQU(PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME, ·d), 'Gut saline medium')) | dp_halftime	nil		ELSE		
C2	dp_halftime.value_y | ht	-		ht > 1.0·d	ELSE	
C3	ByUser(DN_dissolution_outcome_in_fish_gut_saline)	True	False	-	-	
A1	DN_dissolution_outcome_in_fish_gut_saline			very_slow	quick	
A2	**Reset**(DN_dissolution_outcome_in_fish_gut_saline)		X			
		R1	R2	R3	R4	

Defined expressions

name	type	expression	comment
type_category	: String	"nanoform"	
candidate_NFs	: Nanoforms	Nanoforms{self}	
coatings	: Chemicals	chemistry→Select(ch | ch.constituent_role = 'coating')	*All chemical constituents of the nanomaterial having 'coating' as constituent_role.*
shells	: Chemicals	chemistry→Select(ch | ch.constituent_role = 'shell')	*All chemical constituents of the nanomaterial having 'shell as constituent_role.*
organic_coatings	: Chemicals	coatings→Select(c | c.category = 'organic compound')	
shape_category_endpoint	: EP_Records	endpoints→Select(ep | ep.result_endpoint = PC_ASPECT_RATIO_SHAPE::EP_SHAPE_CATEGORY)	
dp_mssa	: EP_DataObject	DP_From(EPQU(PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA, ·$m^2 \cdot g^{-1}$))	
dp_mssa_edit	: EP_DataObject	DP_From(TITLE("Mass Specific Surface Area", EDIT(EPQU(PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA, ·$m^2 \cdot g^{-1}$))))	
dp_aspect_ratio_D3_D1	: EP_DataObject	DP_From(ENUM(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1), slConstituentParticleLevel))	

Operators

```
procedure Nanoform.Initialize() [specialization]
  begin
    /* Each nanoform has initally a chemical constituent. */  ;
    with Add_Constituent(Chemical) | newChemical then
    begin
    end;
    with Add_SizeDistribution() | smallest_sd then
    begin
      smallest_sd.D ?= D1
    end;
    with Add_SizeDistribution() | largest_sd then
    begin
      largest_sd.D ?= D3
    end;
    inherited Initialize()
  end
```

function Nanoform.BI_Qualifiers(): EPQs [specialization]

C1		-
A1	result→Add(TITLE("Constituent particle size, Dn10 for the smallest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D1), slConstituentParticleLevel), 10.0·%)))	X
A2	result→Add(TITLE("Constituent particle size, Dn50 for the smallest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D1), slConstituentParticleLevel), 50.0·%)))	X
A3	result→Add(TITLE("Constituent particle size, Dn90 for the smallest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D1), slConstituentParticleLevel), 90.0·%)))	X
A4	result→Add(TITLE("Constituent particle size, Dn10 for the largest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D3), slConstituentParticleLevel), 10.0·%)))	X
A5	result→Add(TITLE("Constituent particle size, Dn50 for the largest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D3), slConstituentParticleLevel), 50.0·%)))	X
A6	result→Add(TITLE("Constituent particle size, Dn90 for the largest dimension", PER(ENUM(EPQ(PC_GRANULOMETRY::EP_DnPx_D3), slConstituentParticleLevel), 90.0·%)))	X
A7	result→Add(TITLE("Shape category", EPQ(PC_ASPECT_RATIO_SHAPE::EP_SHAPE_CATEGORY)))	X
A8	result→Add(TITLE("Mass Specific Surface Area (MSSA)", EPQ(PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA)))	X
A9	result→Add(TITLE("Aspect Ratio (major/minor axis) of the constituent particles", ENUM(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1), slConstituentParticleLevel)))	X
A10	result→Add(TITLE("Aspect Ratio (minor/major axis) of the constituent particles", ENUM(EPQ(PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3), slConstituentParticleLevel)))	X
		R1

function Nanoform.Create() [specialization]

```
  with self→New | newNM then
  begin
    result := newNM;
    result.Initialize()
  end
```

function Nanoform.ConstituentRoleDomain(composing_context : Material): ConstituentRoles [specialization]

C1	composing_context	Product				Article		ELSE
C2	physical_state	solid	liquid	gas	ELSE	solid	ELSE	-
A1	result→Add('contained')					X	X	
A2	result→Add('surface bound')	X				X		
A3	result→Add('dispersed')	X	X	X		X		
A4	result := composing_context.RoleCombinationsDomain(self, result)	X						
		R1	R2	R3	R4	R5	R6	R7

function Nanoform.PhysicalStateDomain(composing_context : Material): PhysicalStates [specialization]

```
| PhysicalStates{solid, liquid}
```

function Nanoform.GetSubstanceCategories(): SubstanceCategories [specialization]

C1	physical_state	solid	ELSE
A1	result→Add('powder')	X	
		R1	R2

function Nanoform.DerivePhaseSizes(): PhaseSizes [specialization]

```
| PhaseSizes{colloid}
```

Defined composites

Any instance of Nanoform is composed of

- one or more size_distributions of SizeDistribution

Class 'Mono-constituent substance' is kind of Substance

A substance will be considered as mono-constituent if one constituent is present at a concentration of at least 80% (w/w) and the impurities make up no more than 20% (w/w), Intentionally added substances other than those added to stabilise the substance are separate substances that are not to be considered in the main mass balance.

Inference methods

Inference method: 'Infer physical state'

C1	ByUser(physical_state)	False		True
C2	constituents	1	ELSE	-
A1	physical_state	constituents[1].physical_state		
		R1	R2	R3

Defined expressions

name	type	expression	comment
type_category	: String	"mono-constituent substance"	

Operators

```
function 'Mono-constituent substance'.Create() [specialization]
  with self→New | newMCS then
  begin
    result := newMCS;
    with newMCS.Add_Constituent(Chemical) | newChemical then
    begin
    end
  end
```

function 'Mono-constituent substance'.ConstituentRoleDomain(composing_context : Material): ConstituentRoles [specialization]

C1	composing_context	Product				Article		'Mixture'	ELSE
C2	physical_state	solid	liquid	gas	ELSE	solid	ELSE	-	-
A1	result→Add('solid matrix')	X							
A2	result→Add('liquid medium')		X						
A3	result→Add('gaseous medium')			X					
A4	result→Add('mixed')							X	
A5	result→Add('container')					X			
A6	result→Add('contained')					X	X		
A7	result := composing_context.RoleCombinationsDomain(self, result)	X	X	X					
		R1	R2	R3	R4	R5	R6	R7	R8

function 'Mono-constituent substance'.PhysicalStateDomain(composing_context : Material): PhysicalStates [specialization]

C1	constituents	0	1	ELSE
A1	result := PhysicalStates{solid, liquid, gas}	X	X	
		R1	R2	R3

Class 'Multi-constituent substance' is kind of Substance

A substance is defined in REACH by Article 3 and in CLP by Article 2 as:

'a chemical element and its compounds in the natural state or obtained by any manufacturing process,
including any additive necessary to preserve its stability and any impurity deriving from the process used,
but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.'

REACH encompasses substances (mono-constituent, multi-constituent, UVCB substances and 'nanoform' (new!)) which all should be addressed as substances.

Defined expressions

name	type	expression	comment
type_category	: String	"multi-constituent substance"	

Operators

```
function 'Multi-constituent substance'.Create() [specialization]
  with self→New | newMCS then
  begin
    result := newMCS;
    with newMCS.Add_Constituent(Chemical) | newChemical then
    begin
    end;
    with newMCS.Add_Constituent(Chemical) | newChemical then
    begin
    end
  end
```

```
function 'Multi-constituent substance'.ConstituentRoleDomain( composing_context : Material ): ConstituentRoles [specialization]
```

C1	composing_context	Product				Article	'Mixture'	ELSE
C2	physical_state	solid	liquid	gas	ELSE	-	-	-
A1	result→Add('solid matrix')	X				X		
A2	result→Add('liquid medium')		X					
A3	result→Add('gaseous medium')			X				
A4	result→Add('contained')					X		
A5	result→Add('mixed')						X	
		R1	R2	R3	R4	R5	R6	R7

Class 'UVCB substance' is kind of Substance

A substance is defined in REACH by Article 3 and in CLP by Article 2 as:

'a chemical element and its compounds in the natural state or obtained by any manufacturing process,
including any additive necessary to preserve its stability and any impurity deriving from the process used,
but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.'

REACH encompasses substances (mono-constituent, multi-constituent, UVCB substances and 'nanoform' (new!)) which all should be addressed as substances.

Operators

function 'UVCB substance'.ConstituentRoleDomain(composing_context : Material): ConstituentRoles [specialization]

C1	composing_context	Product				Article	'Mixture'	ELSE
C2	physical_state	solid	liquid	gas	ELSE	-	-	-
A1	result→Add('solid matrix')	X				X		
A2	result→Add('liquid medium')		X					
A3	result→Add('gaseous medium')			X				
A4	result→Add('contained')					X		
A5	result→Add('mixed')						X	
		R1	R2	R3	R4	R5	R6	R7

Class **Medium** is kind of **Material**

Abstract medium class, representing all potential external media and test media the targeted material can be in.

Attributes

name	type	domain	inference	comment
pH	: Real	(# ≥ 0) and (# ≤ 14)		

Class **EnvMedium** is kind of **Medium**

Material representing the 'relevant medium' like actcual river water, soil and sediment.

The composition of the different eco media is determined by the specific constituents added. Each zone/field of an environmental compartment has its own eco medium.

Attributes

name	type	domain	inference	comment
temperature	: Real			

Defined expressions

name	type	expression	comment
name_path	: String	env_comp→**If**(c | c.**name** + " | " + type_category, **name**)	
env_comp	: EnvCompartment	zone→**If**(z | z.compartment, **nil**)	

Class **AirMedium** is kind of **EnvMedium**

Eco medium representing the air which can be used in zones of both indoor and outdoor air compartments.

Attributes

name	type	domain	inference	comment
pressure	: Real			

Defined expressions

name	type	expression	comment
type_category	: String	"air medium"	

Class `SoilMedium` is kind of `EnvMedium`

Eco medium used to describe the soil composition and its specific properties.

Attributes

name	type	domain	inference	comment
compaction_class	:: CompactionClass			
packing_density	: Real			*Packing density (p) integrates bulk density, structure and organic matter content to express compactness of soils.*
macro_porosity	: Real			*Can be derived from sand, clay and silt content*

Defined expressions

name	type	expression	comment
type_category	: String	"soil medium"	

Class `SedimentMedium` is kind of `EnvMedium`

Eco medium used to describe the sediment composition and its specific properties.

Attributes

name	type	domain	inference	comment
toxicity_ratio_ion_mol_vs_NF	:: ToxRatioOutcome			

Defined expressions

name	type	expression	comment
type_category	: String	"sediment medium"	

Class `AquaticMedium` is kind of `EnvMedium`

Eco medium representing an aquatic medium like freshwater or marinewater. Besides its composition it also has specific properties like flowtype and flowrate.

Attributes

name	type	domain	inference	comment
flow_type	:: FlowType			
flow_rate	: Real			

Defined expressions

name	type	expression	comment
type_category	: String	"aquatic medium"	

Class `'Simulated natural fresh waters'` is kind of `AquaticMedium`

Simulated natural fresh waters [ISO-TR 19057-2017, 10.4.2].

Class `'Simulated sea water'` is kind of `AquaticMedium`

Simulated sea water [ISO-TR 19057-2017, 10.4.3]

Class `'Simulated estuarine waters'` is kind of `AquaticMedium`

Simulated estuarine waters [ISO-TR 19057-2017, 10.4.4]

Class `BioMedium` is kind of `Medium`

Material representing biological media like (like the lysosomal compartment of a cell).

Class `DispersionMedium` is kind of `Medium`

Abstract medium class, representing all potential external media and test media the targeted material can be in.

Class `Chemical` is kind of `Material`

'A pure chemical compound composed of a single molecule.' [Reach]
Atoms, ions and molecules smaller than 1 nm in all dimensions, larger molecules within the nanoscale are considered nano-objects.
A 'chemical' cannot own constituents of itself anymore.

Attributes

name	type	domain	inference	comment
molecular_formula	: String			
coating_origin	:: CoatingOrigin			
coating_thickness	: Real			*Only relevant in case constituent_role = 'coating', thickness of the coating in nm.*
hazardous_to_aquatic_environment	:: YesNo			

Inference methods

Inference method: 'Infer physical state'

C1	composer as 'Mono-constituent substance' | mono_subst	nil			ELSE	
C2	ByUser(mono_subst.physical_state)	-			True	False
C3	composer is Nanoform	True		False	-	-
C4	ByUser(physical_state)	True	False	-	-	-
A1	physical_state		solid		mono_subst.physical_state	
		R1	R2	R3	R4	R5

Defined expressions

name	type	expression	comment
chemistry	: Chemicals	Chemicals{self}	
type_category	: String	"chemical"	
dissolved_name	: String	(physical_state = ions)→If(name + " [ionic form]", name + " [molecule form]")	

Operators

function Chemical.BI_Qualifiers(): EPQs [specialization]

C1		-
A1	result→Add(TITLE("IUPAC name", EPQ(PC_IDENTITY::ID_IUPAC_**NAME**)))	X
A2	result→Add(TITLE("Type", EPQ(PC_COMPOSITION::EP_CONSTITUENT_ROLE)))	X
A3	result→Add(TITLE("CAS Reg Nr", EPQ(PC_IDENTITY::ID_CAS_REG_NR)))	X
A4	result→Add(TITLE("Category", EPQ(PC_COMPOSITION::EP_COMPOSITION_CATEGORY)))	X
A5	result→Add(TITLE("Mass%", EPQ(PC_COMPOSITION::EP_MASS_CONC)))	X
		R1

function Chemical.Relevant_CategoryEndpoints(): Enumerations [specialization]

C1	physical_state	solid	ELSE
A1	result→Add(PC_IDENTITY)	X	X
A2	result→Add(PC_CLASSIFICATION_LABELING)	X	X
A3	result→Add(PC_COMPOSITION)	X	X
A4	result→Add(PC_CRYSTALLINE_PHASE)	X	
A5	result→Add(PC_CRYSTALLITE_AND_GRAIN_SIZE)	X	
		R1	R2

function Chemical.ConstituentRoleDomain(composing_context : Material): ConstituentRoles [specialization]

C1	composer	Nanoform	'Mono-constituent substance'	'Multi-constituent substance'	Substance	ELSE
A1	result→Add('main chemical')		X	X	X	
A2	result→Add('core')	X				
A3	result→Add('shell')	X				
A4	result→Add('wall')	X				
A5	result→Add('coating')	X				
A6	result→Add('dope')	X				
A7	result→Add('impurity')	X	X	X	X	
A8	result→Add('additive')		X	X	X	
A9	/* Constrains based on role combinations */					
A10	result := composing_context.RoleCombinationsDomain(self, result)			X	X	
		R1	R2	R3	R4	R5

function Chemical.PhysicalStateDomain(composing_context : Material): PhysicalStates [specialization]
```
(composer is Nanoform)→If(PhysicalStates{solid, liquid}, PhysicalStates{ions, solid, liquid, gas})
```

function Chemical.DerivePhaseSizes(): PhaseSizes [specialization]

C1	constituent_role	'dissolved'	'dispersed'				ELSE
C2	physical_state	-	solid	liquid	gas	ELSE	-
A1	result→Add(#)	dissolved	colloid	colloid	coarse		
A2	result→Add(#)		coarse	coarse			
		R1	R2	R3	R4	R5	R6

```
function Chemical.CompositionCategoryDomain(): CompositionCategories [specialization]
| CompositionCategories{'organic compound', 'inorganic compound', 'water'}

function Chemical.Add_CrystallinePhase(): CrystallinePhase
  with CrystallinePhase→New | newCPH then
  begin
    result := newCPH;
    self→AddComponent(crystalline_phases, newCPH);
    result.Initialize()
  end

procedure Chemical.Remove_CrystallinePhase( cph : CrystallinePhase )
  self→RemoveComponent(crystalline_phases, cph)
```

Defined composites

Any instance of `Chemical` is composed of

- one or more `crystalline_phases` of CrystallinePhase

Class `'Mixture'` is kind of `Material`

A mixture is defined in REACH
A mixture consists of several different substances. Each individual component substance in a mixture needs to be identified, and when required registered according to REACH and/or notified according to CLP either by the substance manufacturer or by the importer of the mixture

Defined expressions

name	type	expression	comment
`type_category`	: `String`	`"mixture"`	

Operators

Class `Article` is kind of `Material`

Individual articles/ product items, composed of one or more materials with a quantified amount. At least one 'material' must be added as a constituent. For example: tennis rackets, bumpers, diesel filters, can of paint, tiles, T-shirts, socks, bags filled with powder, sun screen spray. But also, used and articles to be disposed.

"article: means an object which during production is given a special shape, surface or design which determines its function to a greater degree than does its chemical composition" (Article 3(3) of REACH).

Attributes

name	type	domain	inference	comment
`article_category`	:: AC			

Inference methods

Inference method: `'Infer physical state'`

C1		-
A1	`physical_state`	`solid`
		R1

Defined expressions

name	type	expression	comment
`type_category`	: `String`	`"article"`	
`abbreviation`	: `String`	`"ART"`	

Operators

Class `Product` is kind of `Material`

Abstract material, representing both nanomaterials (forms) and other substances and materials in a certain phase.

Attributes

name	type	domain	inference	comment
product_category	:: PC			

Defined expressions

name	type	expression	comment
type_category	: String	"product"	
abbreviation	: String	"PROD"	

Operators

`function` Product.ConstituentRoleDomain(composing_context : Material): ConstituentRoles [specialization]

C1	composing_context	nil	Article			ELSE	
C2	physical_state	-	solid	liquid	gas	ELSE	-
A1	result→Add('solid matrix')		X				
A2	result→Add('contained')		X	X	X		
		R1	R2	R3	R4	R5	R6

Class `MaterialProxy` is kind of `Material`

The material proxy is a conceptual class needed to allow reuse of a defined material as components of articles or nano enabled products.

Inference methods

Inference method: 'Infer name'

C1	original	nil	ELSE
A1	name		original.name
		R1	R2

Inference method: 'Infer physical state'

C1	original	nil	ELSE
A1	physical_state	solid	original.physical_state
		R1	R2

Defined expressions

name	type	expression	comment
chemistry	: Chemicals	original→**If**(o | o.chemistry, Chemicals{})	*The chemisty of the original material.*
surface_chemistry	: Chemicals	original→**If**(o | o.surface_chemistry, Chemicals{})	
core_chemistry	: Chemicals	original→**If**(o | o.core_chemistry, Chemicals{})	
is_particulate	: Boolean	original→**If**(o | o.is_particulate, False)	
type_category	: String	"existing"	
all_constituents	: Materials	original→**If**(o | o.all_constituents, Materials{})	
is_eNanoMapper_substance	: Boolean	original→**If**(o | o.is_eNanoMapper_substance, False)	
v_self	: Material	original	
nano_constituents	: Nanoforms	original→**If**(o | o.nano_constituents, Nanoforms{})	
nano_enabled	: Boolean	original→**If**(o | o.nano_enabled, False)	
abbreviation	: String	"NF/set"	
candidate_NFs	: Nanoforms	(original **is** Nanoform)→**If**(Nanoforms{original **as** Nanoform}, Nanoforms{})	

Operators

```
function MaterialProxy.ConstituentRoleDomain( composing_context : Material ): ConstituentRoles [specialization]
| original→If(o | o.ConstituentRoleDomain(composer), ConstituentRoles{})
```

```
function MaterialProxy.PhysicalStateDomain( composing_context : Material ): PhysicalStates [specialization]
  if original ≠ nil then
    result := original.PhysicalStateDomain(composing_context)
```

```
function MaterialProxy.GetSubstanceCategories(): SubstanceCategories [specialization]
  if original ≠ nil then
  begin
    if composer ≠ nil then
    begin
      /* The proxy has a composer.. so the original material is used as a constituent in another material */    ;
      result := inherited GetSubstanceCategories()
    end
    else
    begin
      /* The proxy has no composer.. so the original material is used as is.. most likely as a powder..   */    ;
      result := original.GetSubstanceCategories()
    end
  end
```

```
function MaterialProxy.DerivePhaseSizes(): PhaseSizes [specialization]
| original→If(o | o.DerivePhaseSizes(), PhaseSizes{})
```

Class **CandidateNFProxy** is kind of **Material**

The candidate NF proxy represents any NF within the provisional set of nanoform to be grouped.

Inference methods

Inference method: 'Infer physical state (candidates NF)'

C1	candidate_NFs.physical_state→Unique | physical_states	0	1	ELSE
A1	physical_state	solid	physical_states[1]	nil
		R1	R2	R3

Inference method: 'Infer name'

C1	ByUser(name)	False	True
A1	name	"the candidate nanoform(s)"	
		R1	R2

Defined expressions

name	type	expression	comment
type_category	: String	"NF candidate(s)"	
abbreviation	: String	"NF(s)"	
candidate_NFs	: Nanoforms	scenario.nanoforms	

Operators

```
function CandidateNFProxy.ConstituentRoleDomain(composing_context : Material ): ConstituentRoles [specialization]
|  candidate_NFs.ConstituentRoleDomain(composing_context)→Sum→Unique
```

```
function CandidateNFProxy.PhysicalStateDomain(composing_context : Material ): PhysicalStates [specialization]
|  candidate_NFs.physical_state→Unique
```

```
function CandidateNFProxy.GetSubstanceCategories(): SubstanceCategories [specialization]
  foreach nf, i of scenario.nanoforms do
  begin
    with nf.GetSubstanceCategories() | nf_categories do
    begin
      if i = 1 then
        result := nf_categories
      else
        result := (result * nf_categories)→AsSequence
    end
  end
```

```
function CandidateNFProxy.DerivePhaseSizes(): PhaseSizes [specialization]
|  candidate_NFs.DerivePhaseSizes()→Sum→Unique
```

Class `CrystallinePhase` is kind of `EP_Owner`

CrystallineForm (phase)
One or more crystalline forms can be used to indicate the (poly)crystallinity of a solid chemical.
Multiple chrystalline forms (including amorphous in addition) can be combined in any percentage adding up to 100%.

Attributes

name	type	domain	inference	comment
crystal_system	:: CrystalSystem		Infer crystal system	
space_group	:: SpaceGroup		Infer space group	*(Crystallographic) space group types (230 in three dimensions). (Wikipedia also used in OECD harmonised templates)*
crystallite_size	: Real			*The size of the crystal unit cell in nm.*
mineral_name	: String			*The 'mineral name' indicates a 'chemical' of a certain crystallinity form. (e.g. rutile, anatase etc. being both TIO2(s) but with different crystal forms and as such with different phys-chem and toxicity properties)*
relative_mass_percentage	: percentage	(# ≥ 0.0·%) and (# ≤ ConcentrationDomain-Max())	Infer relative mass percentage	

Inference methods

Inference method: 'Infer crystal system'

C1	DP_FromProvided(EPQU(PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM, ·%)) | dp_cs	nil	ELSE
A1	**Reset**(crystal_system)	X	
A2	crystal_system		dp_cs.enum_y
		R1	R2

Inference method: 'Infer space group'

C1	DP_FromProvided(EPQU(PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP, ·%)) | dp_spg	nil						ELSE
C2	ByUser(crystal_system)	True					False	-
C3	Current(crystal_system)	'amorphous'	ELSE				-	-
C4	ByUser(space_group)	-	True		False	True	False	-
C5	space_group	-	SpaceGroupDomain()	ELSE	-	-	-	-
A1	space_group	amorphous						dp_spg.enum_y
A2	**Reset**(space_group)	X		X			X	
		R1	R2	R3	R4	R5	R6	R7

Inference method: 'Infer relative mass percentage'

C1	ByUser(relative_mass_percentage)	False	True

A1	**with** chemical.crystalline_phases→Reject(cph | ByUser(cph.relative_mass_percentage))→Size | nr **do**
	begin
	  if nr = 1 **then**
	  relative_mass_percentage != ConcentrationDomainMax()
	  else
	  relative_mass_percentage != 0.0·%
	end
		X	

		R1	R2

Operators

```
function CrystallinePhase.CategoryEndpointDomain(): Enumerations [specialization]
| Enumerations{PC_CRYSTALLITE_AND_GRAIN_SIZE, PC_CRYSTALLINE_PHASE}
```

```
function CrystallinePhase.BI_Qualifiers(): EPQs [specialization]
```

C1		-
A1	result→Add(TITLE("Crystal system", EPQU(PC_CRYSTALLINE_PHASE::EP_CRYSTAL_SYSTEM, ·%)))	
A2	result→Add(TITLE("Space group", EPQU(PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP, ·%)))	X
A3	result→Add(TITLE("Mineral name", EPQ(PC_CRYSTALLINE_PHASE::EP_MINERAL_NAME)))	X
A4	result→Add(TITLE("Crystallite size", EPQ(PC_CRYSTALLITE_AND_GRAIN_SIZE::EP_CRYSTALLITE_SIZE)))	X
		R1

```
function CrystallinePhase.DP_From(epq : EP_Qualifier): EP_DataObject [specialization]
  begin
    /* Find qualified material basic information datapoint */  ;
    begin
    end;
    /* Find decision node derived endpoint records */  ;
    if result = nil then
      with DP_FromProvided(epq) | estimate_dp then
      begin
        result := estimate_dp
      end
  end
```

```
function CrystallinePhase.SpaceGroupDomain(): SpaceGroups
```

C1	Known(crystal_system)	True								False
C2	crystal_system	'amorphous'	'triclinic'	'monoclinic'	'orthorhombic'	'tetragonal'	'trigonal'	'hexagonal'	'cubic'	ELSE	-
A1	result := SpaceGroup→Enumerates									X	X
A2	foreach i of # do result→Add(SpaceGroup[i])		[1 to 2]	[3 to 15]	[16 to 74]	[75 to 142]	[143 to 167]	[168 to 194]	[195 to 230]	[1 to 230]	[1 to 230]
A3	result→Add(amorphous)	X									
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

```
function CrystallinePhase.ConcentrationDomainMax(): percentage
  if chemical ≠ nil then
  begin
    with chemical.crystalline_phases→Excluding(self)→Select(cph | ByUser(cph.relative_mass_percentage)).relative_mass_percentage→Sum | percentage_set do
    begin
      with (100.0·% - percentage_set)→Max(0.0·%) | percentage_left do
      begin
        result := percentage_left
      end
    end
  end
  else
  begin
  end
```

Class SizeDistribution

Attributes

name	type	domain	inference	comment
D	:: Dimension			

Defined expressions

name	type	expression	comment
DP_DnP10	: EP_DataObject	(D = D1)→**If**(nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D1), 10.0·%))), nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D3), 10.0·%))))	
DP_DnP50	: EP_DataObject	(D = D1)→**If**(nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D1), 50.0·%))), nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D3), 50.0·%))))	
DP_DnP90	: EP_DataObject	(D = D1)→**If**(nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D1), 90.0·%))), nanoform.DP_FromProvided(EDIT(PER(EPQ(PC_GRANULOMETRY::EP_DnPx_ D3), 90.0·%))))	

4.3 Defined associations

Association `medium_interaction`

To deal with medium specific properties

- zero or more relevant_materials of any kind of Material
- zero or more relevant_media of any kind of Medium

Attributes

name	type	domain	inference	comment
DN_dissolution_in_medium_outcome	:: DissolutionOutcome		TTS dissolution outcome in relevant medium	*DN-EG1-1*
DN_dissolution_in_medium_TL	:: TierLevel			
DN_dispersion_stability_in_medium_outcome	:: DispersionOutcome		TTS dispersion stability outcome in relevant medium	
DN_dispersion_stability_in_medium_TL	:: TierLevel			
DN_biodegradable_organic_coatings_present	:: YesNo		TTS organic_coatings_are_biodegradable	
DN_biodegradable_organic_coatings_present_TL	:: TierLevel			
DN_biodegradable_organic_coatings	: Chemicals			
DN_solutes_remain_their_form	:: YesNo			
DN_solutes_remain_their_form_TL	:: TierLevel			
DN_NFs_remain_their_form	:: YesNo			
DN_NFs_remain_their_form_TL	:: TierLevel			
DN_affinity_to_solid_soil_phase	:: AffinityOutcome			
DN_affinity_to_solid_soil_phase_TL	:: TierLevel			
DN_toxicity_ratio_ion_mol_vs_NF	:: ToxRatioOutcome			
DN_toxicity_ratio_ion_mol_vs_NF_TL	:: TierLevel			

Association `represents`

- at most one original of any kind of Material
- zero or more proxies of MaterialProxy

4.4 Defined collections

Chemicals defines a sequence containing Chemical objects.
MaterialFunctions defines a sequence containing MaterialFunction enumerates.
Materials defines a sequence containing any kind of Material objects.
MaterialClasses defines a sequence containing any kind of Material types.
ConstituentRoles defines a sequence containing ConstituentRole enumerates.
NanoformClasses defines a sequence containing Nanoform types.
PhysicalStates defines a sequence containing PhysicalState enumerates.
Nanoforms defines a sequence containing Nanoform objects.
SubstanceCategories defines a sequence containing SubstanceCategory enumerates.
PhaseSizes defines a sequence containing PhaseSize enumerates.
ShapeCategories defines a sequence containing ShapeCategory enumerates.
CompositionCategories defines a sequence containing CompositionCategory enumerates.
SpaceGroups defines a sequence containing SpaceGroup enumerates.

Defined expressions

name	type	expression	comment
casnr_RegExpr	: String	"^[1-9]{1}\d{1,6}-\d{2}-\d$"	

Operators

```
function MATERIAL_KB::IsValidCASnumber( cas_number : String ):: Boolean
| cas_number→Matches(casnr_RegExpr) and HasValidCASnumber_Checksum(cas_number)
```

```
function MATERIAL_KB::DeriveMixtureCategory( dis_phase :: PhysicalState, con_phase :: PhysicalState, dis_size :: PhaseSize ):: SubstanceCategory
```

C1	con_phase	gas									liquid										solid									ELSE	
C2	dis_phase	ions	gas	liquid		solid				ELSE	ions	gas	liquid		solid				ELSE	ions	gas		liquid			solid			ELSE	-
C3	dis_size	-	-	dissolved	ELSE	dissolved	colloid	coarse	ELSE	-	-	dissolved	ELSE	dissolved	ELSE	dissolved	colloid	coarse	ELSE	-	-	dissolved	ELSE	dis-solved	colloid	ELSE	dissolved	colloid	coarse	ELSE	-	-
A1	result	'gas'	'gas mixture'	'liquid'	'aerosol'	'gas'	'solid aerosol'	'solid aerosol, dust'	'none'	'none'	'liquid solution'	'liquid solution'	'fluid foam'	'liquid solution'	'emulsion'	'liquid solution'	'sol'	'suspension'	'suspension'	'none'	'solid'	'solid solution'	'solid foam'	'solid solu-tion'	'gel'	'none'	'solid solution'	'solid sol'	'solid mixture'	'solid mix-ture'	'none'	'none'
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21	R22	R23	R24	R25	R26	R27	R28	R29	R30	R31

```
function MATERIAL_KB::ShapeCategoryToStr( sc :: ShapeCategory ):: String
  case sc of
    scSpheroidal:
      result := "spheroidal";
    scElongated:
      result := "elongated";
    scPlatelets:
      result := "platelets"
    else
      result := "?"
  end
```

```
function MATERIAL_KB::SpaceGroupNrToStr( sg : Integer ):: String
  if (sg ≥ 1) and (sg ≤ 230) then
    result := Strings{"P1", "P1", "P2", "₁P2", "C2", "Pm", "Pc", "Cm", "Cc", "P2/m", "₁P2/m", "C2/m", "P2/c", "₁P2/c", "C2/c", "P222", "₁P222", "₁₁P222", "₁₁₁P222", "₁C222", "C222", "F222", "I222", "₁₁₁I222", "Pmm2",
      "₁Pmc2", "Pcc2", "Pma2", "₁Pca2", "Pnc2", "₁Pmn2", "Pba2", "₁Pna2", "Pnn2", "Cmm2", "₁Cmc2", "Ccc2", "Amm2", "Aem2", "Ama2", "Aea2", "Fmm2", "Fdd2", "Imm2", "Iba2", "Ima2", "Pmmm", "Pnnn", "Pccm", "Pban", "Pmma"
      , "Pnna", "Pmna", "Pcca", "Pbam", "Pccn", "Pbcm", "Pnnm", "Pmmn", "Pbcn", "Pbca", "Pnma", "Cmcm", "Cmca", "Cmmm", "Cccm", "Cmme", "Ccce", "Fmmm", "Fddd", "Immm", "Ibam", "Ibca", "Imma", "P4", "₁P4", "₂P4", "₃P4"
      , "I4", "₁I4", "P4", "I4", "P4/m", "₂P4/m", "P4/n", "₂P4/n", "I4/m", "₁I4/a", "P422", "₁P422", "₁P422", "₁₁P422", "₂P422", "₂₁P422", "₃P422", "₃₁P422", "I422", "₁I422", "P4mm", "P4bm", "₂P4cm", "₂P4nm", "P4cc",
      "P4nc", "₂P4mc", "₂P4bc", "I4mm", "I4cm", "₁I4md", "₁I4cd", "P42m", "P42c", "₁P42m", "₁P42c", "P4m2", "P4c2", "P4b2", "P4n2", "I4m2", "I4c2", "I42m", "I42d", "P4/mmm", "P4/mcc", "P4/nbm", "P4/nnc", "P4/mbm", "P4
      /mnc", "P4/nmm", "P4/ncc", "₂P4/mmc", "₂P4/mcm", "₂P4/nbc", "₂P4/nnm", "₂P4/mbc", "₂P4/mnm", "₂P4/nmc", "₂P4/ncm", "I4/mmm", "I4/mcm", "₁I4/amd", "₁I4/acd", "P3", "₁P3", "₂P3", "R3", "P3", "R3", "P312", "P321",
      "₁P312", "₁P321", "₂P312", "₂P321", "R32", "P3m1", "P31m", "P3c1", "P31c", "R3m", "R3c", "P31m", "P31c", "P3m1", "P3c1", "R3m", "R3c", "P6", "₁P6", "₅P6", "₂P6", "₄P6", "₃P6", "P6", "P6/m", "P63/m", "P622", "
      ₁P622", "₅P622", "₂P622", "₄P622", "₃P622", "P6mm", "P6cc", "₃P6cm", "₃P6mc", "P6m2", "P6c2", "P62m", "P62c", "P6/mmm", "P6/mcc", "₃P6/mcm", "₃P6/mmc", "P23", "F23", "I23", "₁P23", "₁I23", "Pm3", "Pn3", "Fm3", "
      Fd3", "Im3", "Pa3", "Ia3", "P432", "₂P432", "F432", "₁F432", "I432", "₃P432", "₁P432", "₁I432", "P43m", "F43m", "I43m", "P43n", "F43c", "I43d", "Pm3m", "Pn3n", "Pm3n", "Pn3m", "Fm3m", "Fm3c", "Fd3m", "Fd3c", "
      Im3m", "Ia3d"}[sg] + " (nr=" + sg→AsString + ")"
  else
    result := "?"
```

```
function MATERIAL_KB::SpaceGroupToStr( spg :: SpaceGroup ):: String
  with spg→IndexOf | nr then
  begin
    if nr = 231 then
      result := "Amorphous"
    else
      result := SpaceGroupNrToStr(nr)
  end
  else
    result := "?"
```

```
function MATERIAL_KB::SpaceGroupToCrystalSystem( sg :: SpaceGroup ):: CrystalSystem
```

C1	sg	nil	ELSE							
C2	sg→IndexOf	-	# ≤ 2	# ≤ 15	# ≤ 74	# ≤ 142	# ≤ 167	# ≤ 194	# ≤ 230	ELSE
A1	result	'amorphous'	'triclinic'	'monoclinic'	'orthorhombic'	'tetragonal'	'trigonal'	'hexagonal'	'cubic'	'amorphous'
		R1	R2	R3	R4	R5	R6	R7	R8	R9

```
function MATERIAL_KB::CompositionCategoryToStr( cc :: CompositionCategory ):: String
  case cc of
    'organic compound':
      result := "organic compound";
    'organic matter':
      result := "organic matter";
    'inorganic compound':
      result := "inorganic compound";
    'inorganic matter':
      result := "inorganic matter";
    'hybrid material':
      result := "hybrid material";
    'mixture':
      result := "mixture";
    'water':
      result := "water"
    else
      result := "?"
  end
```

```
function MATERIAL_KB::DeriveStateFromSubstanceCategory( sc :: SubstanceCategory ):: PhysicalState
  case sc of
    'gas', 'gas mixture', 'aerosol', 'solid aerosol', 'solid aerosol, dust':
      result := gas;
    'liquid', 'liquid solution', 'fluid foam', 'emulsion', 'suspension', 'sol':
      result := liquid;
    'solid', 'solid solution', 'solid foam', 'gel', 'solid sol', 'solid mixture', 'composite', SubstanceCategory::'capsule':
      result := solid
    else
      result := nil
  end
```

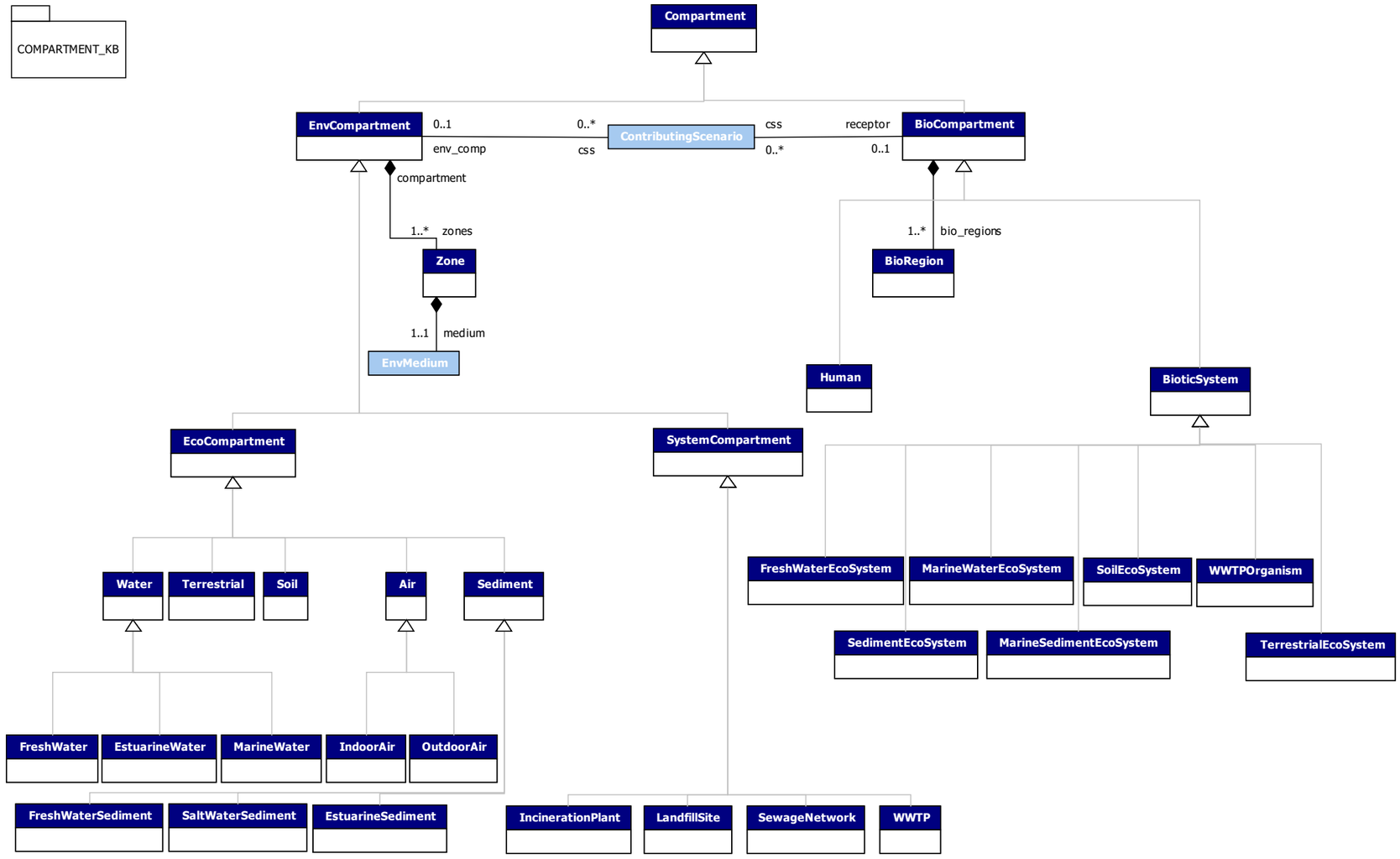
```
function MATERIAL_KB::NF_Appearance( host_material : Material, nf : Nanoform ):: NanoFormManifestations
```

C1	nf	nil	ELSE				
C2	host_material	-	nil	ELSE			
C3	nf in host_material.candidate_NFs	-	-	True	False		
C4	host_material.constituents→Select(c | nf in c.candidate_NFs) | nano_constituent	-	-	-	0	1	ELSE
A1	result→Add(#)			as_powder			
		R1	R2	R3	R4	R5	R6

```
function MATERIAL_KB::ParticleSizeLevelToStr( psl :: ParticleSizeLevel ):: String
  case psl of
    slConstituentParticleLevel:
      result := "const. level";
    slAgglomerateLevel:
      result := "aggl. level"
  end


function MATERIAL_KB::MapSubstanceTypeOntoNMCode( str : String ):: SubstanceType
  case str→Trim of
    "CHEBI_33128":
      result := FULLERENES;
    "NPO_354":
      result := NP_MWCNT;
    "NPO_943":
      result := NP_SWCNT;
    "NPO_735":
      result := NP_DENDRIMERS;
    "ENM_9000007":
      result := NP_NANOCLAY;
    "ENM_9000006":
      result := NP_CERIUM_OXIDE;
    "NPO_1550":
      result := NP_IRON_TRIOXIDE;
    "NPO_1373":
      result := NP_SILICON_DIOXIDE;
    "CHEBI_51050":
      result := NP_TITANIUM_DIOXIDE;
    "CHEBI_133326":
      result := NP_BARIUM_SULFATE;
    "NPO_1542":
      result := NP_ZINC_OXIDE;
    "NPO_401":
      result := NP_GOLD;
    "NPO_1892":
      result := NP_SILVER;
    "ENM_9000200":
      result := NP_IRON;
    "ENM_9000005":
      result := NP_ALUMINIUM_OXIDE;
    "CHEBI_133349":
      result := NP_FIBRILLAR_CELLULOSE;
    "CHEBI_18246":
      result := CELLULOSE;
    "CHEBI_133602":
      result := NP_CARBON_BLACK;
    "ENM_9000073":
      begin
        /* Perhaps not correct ontology entry, only MANGANESE .. not TRIOXIDE*/      ;
        result := NP_MANGANESE_TRIOXIDE
      end
  end
```

Chapter 5 COMPARTMENT_KB



5.1 Defined enumerations

`HumanCategory`

- `'worker'`
- `'consumer'`
- `'bystander'`

5.2 Defined classes

Class `Compartment`

Attributes

name	type	domain	inference	comment
name	: String			

Defined expressions

name	type	expression	comment
type_name	: String	"Compartment"	

Operators

```
constructor Compartment.Create()
|  self→New

procedure Compartment.Initialize()
  /* TO BE OVERRIDDEN */
```

Class `EnvCompartment` is kind of `Compartment`

Each environmental compartment has one or more zones representing different fields or regions within it. A zone can either be virtual or physical.
- A virtual zone is used to separate a room in different fields (NEAR FIELD, FAR FIELD) or a river in different segments.
- A physical zone is used to separate different media classes within the same environmental compartment. (e.g. air in room and floor in room)

Defined expressions

name	type	expression	comment
type_name	: String	"Environmental compartment"	

Operators

```
procedure EnvCompartment.Initialize() [specialization]
  Add_Zone()

procedure EnvCompartment.Add_Zone()
  with Zone.Create() | newZone then
    self→AddComponent(zones, newZone)
```

Defined composites

Any instance of `EnvCompartment` is composed of
- one or more `zones` of Zone *Each environmental compartment has one ore more zones representing different fields or regions within it. A zone can either be virtual or physical.*
  - A virtual zone is used to separate a room in different fields (NEAR FIELD, FAR FIELD) or a river in different segments.
  - A physical zone is used to separate different media classes within the same environmental compartment. (eg air in room and floor in room)

Class `EcoCompartment` is kind of `EnvCompartment`

An eco compartment is a natural environmental compartment. (except perhaps for IndoorAir)

Class `Air` is kind of `EcoCompartment`

An abstract air compartment.

Defined expressions

name	type	expression	comment
type_name	: String	"air compartment"	

Class `OutdoorAir` is kind of `Air`

Representing the outdoor air. Sunlight, wind and rain etc..

Defined expressions

name	type	expression	comment
type_name	: String	"Air, outdoor"	

Operators

```
procedure OutdoorAir.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_air_zone then
    begin
      main_air_zone.Add_Medium(AirMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `IndoorAir` is kind of `Air`

Representing a room of certain dimensions. (perhaps to be derived from system compartments?)

Attributes

name	type	domain	inference	comment
background_particle_conc	: particle_conc	# > 0.0·cm^{-3}		
background_particle_size	: Length	# > 0.0·nm		

Defined expressions

name	type	expression	comment
type_name	: String	"Air, indoor"	

Operators

```
procedure IndoorAir.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_air_zone then
    begin
      main_air_zone.Add_Medium(AirMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `Water` is kind of `EcoCompartment`

Abstract class representing any natural water compartment.

Class `FreshWater` is kind of `Water`

A freshwater river or lake.

Defined expressions

name	type	expression	comment
type_name	: String	"Aquatic, fresh water"	

Operators

```
procedure FreshWater.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_aquatic_zone then
    begin
      main_aquatic_zone.Add_Medium(AquaticMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `MarineWater` is kind of `Water`

Salt water system, sea, ocean.

Defined expressions

name	type	expression	comment
type_name	: String	"Aquatic, marine water"	

Operators

```
procedure MarineWater.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_aquatic_zone then
    begin
      main_aquatic_zone.Add_Medium(AquaticMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `EstuarineWater` is kind of `Water`

Brackish water systems

Defined expressions

name	type	expression	comment
type_name	: String	"Aquatic, estuarine water"	

Operators

```
procedure EstuarineWater.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_aquatic_zone then
    begin
      main_aquatic_zone.Add_Medium(AquaticMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `Soil` is kind of `EcoCompartment`

Representing the soil with certain dimensions.

Defined expressions

name	type	expression	comment
type_name	: String	"Soil"	

Operators

```
procedure Soil.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_soil_zone then
    begin
      main_soil_zone.Add_Medium(SoilMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `Sediment` is kind of `EcoCompartment`

Abstract class for natural sediment compartments.

Class `FreshWaterSediment` is kind of `Sediment`

Sediment in a lake or river.

Defined expressions

name	type	expression	comment
type_name	: String	"Sediment, fresh water"	

Operators

```
procedure FreshWaterSediment.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_sediment_zone then
    begin
      main_sediment_zone.Add_Medium(SedimentMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `SaltWaterSediment` is kind of `Sediment`

Sediment in sea, ocean.

Defined expressions

name	type	expression	comment
type_name	: String	"Sediment, salt water"	

Operators

```
procedure SaltWaterSediment.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_sediment_zone then
    begin
      main_sediment_zone.Add_Medium(SedimentMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `EstuarineSediment` is kind of `Sediment`

Sediment in a estuarine environment.

Defined expressions

name	type	expression	comment
type_name	: String	"Sediment, estuarine water"	

Operators

```
procedure EstuarineSediment.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_sediment_zone then
    begin
      main_sediment_zone.Add_Medium(SedimentMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `Terrestrial` is kind of `EcoCompartment`

Natural compartment representing land where plants and animals live.

Defined expressions

name	type	expression	comment
type_name	: String	"Terrestrial"	

Class `SystemCompartment` is kind of `EnvCompartment`

Any man made compartment.

Class `WWTP` is kind of `SystemCompartment`

Waste Water Treatment Plant

Defined expressions

name	type	expression	comment
type_name	: String	"Waste water treatment plant (WWTP)"	

Operators

```
procedure WWTP.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_aquatic_zone then
    begin
      main_aquatic_zone.Add_Medium(AquaticMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `SewageNetwork` is kind of `SystemCompartment`

Sewage network

Defined expressions

name	type	expression	comment
type_name	: String	"Waste water, sewage network"	

Operators

```
procedure SewageNetwork.Initialize() [specialization]
  begin
    inherited Initialize();
    with zones→First | main_aquatic_zone then
    begin
      main_aquatic_zone.Add_Medium(AquaticMedium);
      /*main_air_zone.OnChange_CompositionType(nil, zcAir)*/
    end
  end
```

Class `LandfillSite` is kind of `SystemCompartment`

Landfill site, were final waste is dumped in.

Defined expressions

name	type	expression	comment
type_name	: String	"Landfill site"	

Class `IncinerationPlant` is kind of `SystemCompartment`

Factory where final waste is incinerated.

Defined expressions

name	type	expression	comment
type_name	: String	"Incineration plant"	

Class `BioCompartment` is kind of `Compartment`

Defined expressions

name	type	expression	comment
type_name	: String	"Bio compartment"	
derived_name	: String	name→If(str | str, type_name)	

Operators

```
procedure BioCompartment.Add_BioRegion()
  self→AddComponent(bio_regions, BioRegion)
```

Defined composites

Any instance of BioCompartment is composed of
- one or more bio_regions of BioRegion

Class `Human` is kind of `BioCompartment`

Attributes

name	type	domain	inference	comment
category	:: HumanCategory			

Defined expressions

name	type	expression	comment
type_name	: String	"human"	

Class `BioticSystem` is kind of `BioCompartment`

The specific eco system present in a zone of an eco compartment.

Class `FreshWaterEcoSystem` is kind of `BioticSystem`

The fresh water eco system representing all kind of aquatic species of different trophic levels in lakes and rivers.

Defined expressions

name	type	expression	comment
type_name	: String	"fresh water species"	

Class `MarineWaterEcoSystem` is kind of `BioticSystem`

The marine water eco system representing all kind of aquatic species of different trophic levels living in saltwater seas and oceans.

Defined expressions

name	type	expression	comment
type_name	: String	"marine eco system"	

Class `SoilEcoSystem` is kind of `BioticSystem`

The soil organisms representing all kind of soil related species of different trophic levels.

Defined expressions

name	type	expression	comment
type_name	: String	"soil eco system"	

Class `SedimentEcoSystem` is kind of `BioticSystem`

The fresh water sediment organisms representing all kind of sediment related species of different trophic levels.

Defined expressions

name	type	expression	comment
type_name	: String	"fresh water sediment eco system"	

Class `MarineSedimentEcoSystem` is kind of `BioticSystem`

The salt water sediment organisms representing all kind of sediment related species of different trophic levels.

Defined expressions

name	type	expression	comment
type_name	: String	"marine sediment eco system"	

Class `WWTPOrganism` is kind of `BioticSystem`

The bioorganisms used in waste water treatment plants (WWTP).

Defined expressions

name	type	expression	comment
type_name	: String	"wwtp organisms"	

Class `TerrestrialEcoSystem` is kind of `BioticSystem`

The eco system of plants, animals (including birds?) and microorganisms living on land.

Defined expressions

name	type	expression	comment
type_name	: String	"terrestrial eco system"	

Class `Zone`

A specific region/field within a environmental compartment of a certain environmental medium. For example, a NEAR field in a room, a section within a river.

Attributes

name	type	domain	inference	comment
description	: String		Infer description	

Inference methods

Inference method: 'Infer description'

C1	ByUser(description)	False		True
C2	medium	nil	ELSE	-
A1	description		medium.type_category	
		R1	R2	R3

Defined expressions

name	type	expression	comment
name_path	: String	compartment→**If**(c | c.**name** + description→**If**(s | " | " + s, ""), description)	*The name of the zone preceeded with the compartment name.*

Operators

```
constructor Zone.Create()
  with Zone→New | newZone then
  begin
    result := newZone
  end

procedure Zone.Add_Medium( medium_class :: EnvMedium )
  with medium_class.Create() | newMedium then
  begin
    self→AddComponent(medium, newMedium);
    newMedium.Initialize()
  end
```

Defined composites

Any instance of Zone is composed of
- exactly one medium of any kind of EnvMedium

Class BioRegion

A specific region within a bio compartment of a certain biological medium. Think of alveolar region within the lung etc..

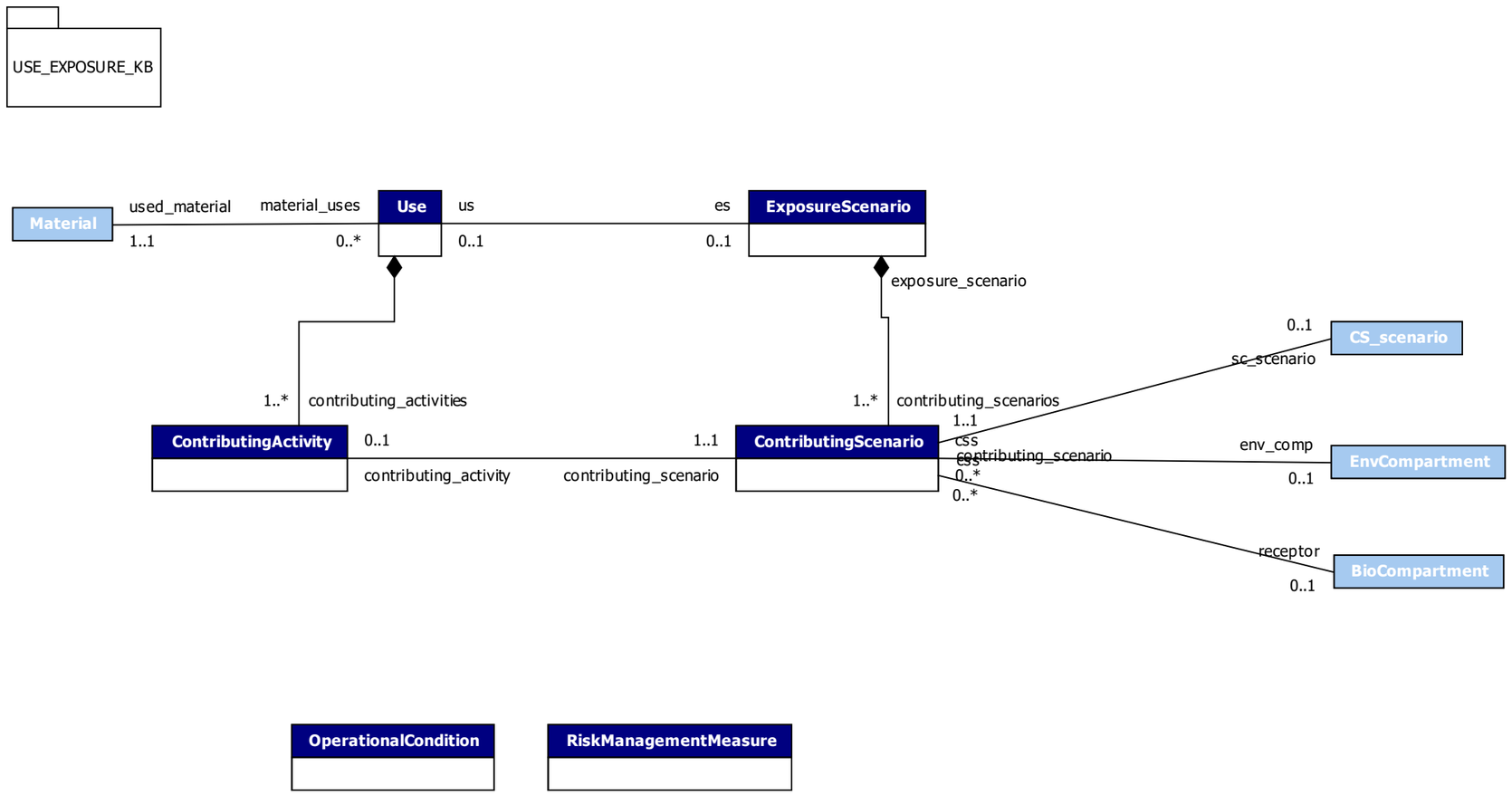
Attributes

name	type	domain	inference	comment
description	: String			

5.3 Defined collections

EnvCompartmentClasses defines a sequence containing any kind of EnvCompartment types.
EnvCompartments defines a sequence containing any kind of EnvCompartment objects.
BioCompartmentClasses defines a sequence containing any kind of BioCompartment types.
BioCompartments defines a sequence containing any kind of BioCompartment objects.

Chapter 6 USE_EXPOSURE_KB



6.1 Defined enumerations

`ExposureRoute`

- `inhalation`
- `dermal`
- `oral`

`ExposureTimeIndicator`

- `peak`
- `'long-term'`

`NF_UseForm`

Indicates how the nanoform is processed or contained in the hosting material, in suspension, as powder or embedded in a solid matrix..

- `in_suspension`
  the nanoform is dispersed in a liquid (suspension) when used
- `as_powder`
  the nanoform is used as a powder

- in_solid_matrix
  the nanoform is used while being embedded in a solid matrix
- bound_to_surface
  the nanoform is used while being bound to a surface
- as_aerosol

MaterialAppearance

The form in which a material is processed/used in a contributing activity.

- maSolidObject
  The material is a solid object with a size > 10 mm. => SolidSizeCategory::'solid object'
- maFirmGranulates
- maPowder
  A powder < 100 µm
- maLiquid
- maGas

CA_Perspective

Contributing Activity Perspective

- environmental
- occupational
- consumer

EnergyLevel

- el_very_high
- el_high
- el_medium
- el_low
- el_very_low
- el_none

6.2 Defined classes

Class Use

The REACH definition of use is given in Article 3, point 24: use: any processing, formulation, consumption, storage, keeping, treatment, filling into containers, transfer from one container to another, mixing, production of an article or any other utilisation.

Attributes

name	type	domain	inference	comment
name	: String			*R.12.4.2.2 Use name*
description	: String			*R.12.4.2.2 Use name and further description of use*
life_cycle_stage	:: LCS			
sector_of_use_category	:: SU			

Defined expressions

name	type	expression	comment
article_category	:: AC	used_material→**If**(m | (m **as** Article)→**If**(ac | ac.article_category, **nil**), **nil**)	
product_category	:: PC	used_material→**If**(m | (m **as** Product)→**If**(pr | pr.product_category, **nil**), **nil**)	
used_material_appearance	:: MaterialAppearance	Derive_MaterialAppearence()	

Operators

function Use.NF_useForm(nf : Nanoform): NF_UseForm

C1	used_material	nil	ELSE									
C2	nf in used_material.candidate_NFs	-	True	False								
C3	used_material.constituents→Select(c | nf in c.candidate_NFs) | nanoconstituents	-	-	0	1							ELSE
C4	nanoconstituents[1].constituent_role	-	-	-	'dispersed'				'surface bound'	'mixed'	ELSE	-
C5	used_material.GetSubstanceCategories()	-	-	-	'sol'	'solid sol'	'solid aerosol'	ELSE	-	-	-	-
A1	result	nil	as_powder	nil	in_suspension	in_solid_matrix	as_aerosol	nil	bound_to_surface			
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11

function Use.Derive_MaterialAppearence(): MaterialAppearance

C1	used_material	nil	CandidateNFProxy	Article	ELSE						
C2	used_material.GetSubstanceCategories() | substance_categories	-	-	-	0	1					ELSE
C3	substance_categories[1]	-	-	-	-	'solid', 'composite', 'solid sol'	'powder'	'liquid', 'sol', 'suspension'	'gas', 'gas mixture', 'aerosol', 'solid aerosol', 'solid aerosol, dust'	ELSE	-
A1	result		maPowder	maSolidObject		maSolidObject	maPowder	maLiquid	maGas		
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10

Defined composites

Any instance of Use is composed of
- one or more contributing_activities of ContributingActivity

Class ContributingActivity

A a use contributing activity / process

Attributes

name	type	domain	inference	comment
name	: String			
erc_code	:: ERC		Infer environmental release category	
proc_code	:: PROC			
ca_perspective	:: CA_Perspective			
ca_category	:: any Enumeration		Infer contributing activity category	
ca_descriptor	:: any Enumerate		Infer contributing activity descriptor	*The specific contributing activity class, see Activity KB*
energy_level	:: EnergyLevel			

Inference methods

Inference method: 'Infer environmental release category'

C1	ByUser(erc_code)	False			True
C2	ERC_Domain(use.life_cycle_stage) | domain	1	ELSE		-
C3	Current(erc_code) in domain	-	True	False	-
A1	erc_code	domain[1]			
A2	**Reset**(erc_code)			X	
		R1	R2	R3	R4

Inference method: 'Infer contributing activity category'

C1	ByUser(ca_category)	False				True		
C2	Potential_AC_Categories(self) | domain	0	1	ELSE		0	ELSE	
C3	Current(ca_category) in domain	-	-	True	False	-	True	False
A1	ca_category		domain[1]					
A2	**Reset**(ca_category)	X			X	X		X
		R1	R2	R3	R4	R5	R6	R7

Inference method: 'Infer contributing activity descriptor'

C1	ca_category	nil	ELSE						
C2	ByUser(ca_descriptor)	-	False				True		
C3	ca_category→Enumerates | domain	-	0	1	ELSE		0	ELSE	
C4	Current(ca_descriptor) in domain	-	-	-	True	False	-	True	False
A1	ca_descriptor			domain[1]					
A2	**Reset**(ca_descriptor)	X	X			X	X		X
		R1	R2	R3	R4	R5	R6	R7	R8

Defined expressions

name	type	expression	comment
title	: String	"Contributing Activity"	
derived_name	: String	use.**name** + " | " + **name**	
descriptor	: String	(ca_perspective = environmental)→**If**(erc_code→**If**(c | c→AsString, "?"), proc_ code→**If**(c | c→AsString, "?"))	

Class **ExposureScenario**

Attributes

name	type	domain	inference	comment
name	: String		Infer name	

Inference methods

Inference method: 'Infer name'

C1	us	nil	ELSE
A1	name		"ES " + us.name
		R1	R2

Defined expressions

name	type	expression	comment
derived_name	: String	**name**	
contributing_activities	: ContributingActivities	contributing_scenarios.contributing_activity→Excluding(**nil**)	
use	: Use	contributing_activities→**If**(cas | cas[1].use, **nil**)	

Defined composites

Any instance of ExposureScenario is composed of
- one or more contributing_scenarios of ContributingScenario

Class ContributingScenario

Attributes

name	type	domain	inference	comment
name	: String		Infer name	
emission_source_segregated_from_receptor	:: YesNo			
enclosed_activity	:: YesNo			
closed_when_NF_is_inside	:: YesNo			
open_during_handling	:: YesNo			*to be deprecated*
PPE_worn	:: YesNo			
potential_splashes_spills	:: YesNo			
localized_extraction_ventilation_used	:: YesNo			
respiratory_protection_equipment_used	:: YesNo			

Inference methods

Inference method: 'Infer name'

C1	contributing_activity | ca	nil	ELSE
C2		-	-
A1	name		ca.name
		R1	R2

Defined expressions

name	type	expression	comment
use	: Use	contributing_activity→**If**(ca | ca.use, **nil**)	
used_material	: Material	use→**If**(u | u.used_material, **nil**)	
candidate_nanoforms	: Nanoforms	used_material→**If**(m | m.scenario.nanoforms, Nanoforms{})	
medium	: EnvMedium	env_comp→**If**(c | c.zones→**If**(z | z[1].medium, **nil**), **nil**)	*Only one zone per env. compartment*
likely_routes_of_exposure	: ExposureRoutesSet	self~receptor→**If**(r | r.routes, ExposureRoutesSet{})	*Likely routes of exposure derived by the hypothesis*
ca_perspective	:: CA_Perspective	contributing_activity→**If**(ca | ca.ca_perspective, **nil**)	
erc_code	:: ERC	contributing_activity→**If**(ca | ca.erc_code, **nil**)	
proc_code	:: PROC	contributing_activity→**If**(ca | ca.proc_code, **nil**)	
ca_category	:: any Enumeration	contributing_activity→**If**(ca | ca.ca_category, **nil**)	
ca_descriptor	:: any Enumerate	contributing_activity→**If**(ca | ca.ca_descriptor, **nil**)	
ca_energy_level	:: EnergyLevel	contributing_activity→**If**(ca | ca.energy_level, el_none)	

Class `OperationalCondition`

OCs

Class `RiskManagementMeasure`

RMM

6.3 Defined associations

Association `corresponds`

- exactly one contributing_scenario of ContributingScenario
- at most one contributing_activity of ContributingActivity

Association `release`

- zero or more css of ContributingScenario
- at most one env_comp of any kind of EnvCompartment

Association `exposure`

- zero or more css of ContributingScenario
- at most one receptor of any kind of BioCompartment

Attributes

name	type	domain	inference	comment
routes	: ExposureRoutesSet			

Association `used`

- exactly one used_material of any kind of Material
- zero or more material_uses of Use

Association `corresponding`

- at most one us of Use
- at most one es of ExposureScenario

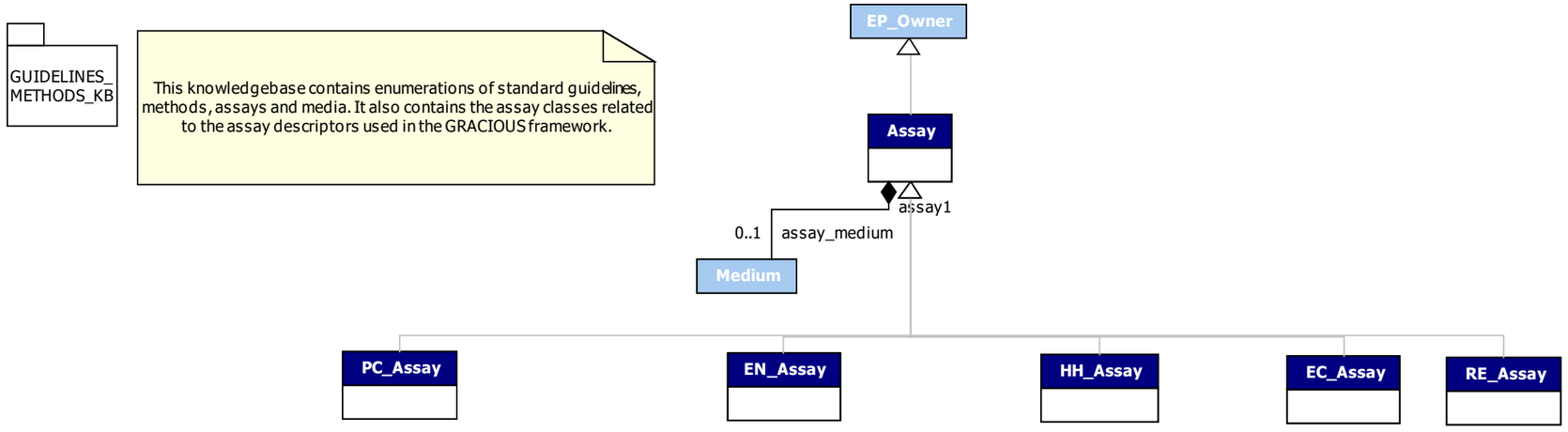
6.4 Defined collections

ExposureRoutes `defines a sequence containing` ExposureRoute `enumerates.`
ExposureScenarios `defines a sequence containing` ExposureScenario `objects.`
ContributingActivities `defines a sequence containing` ContributingActivity `objects.`
ContributingScenarios `defines a sequence containing` ContributingScenario `objects.`
CA_Perspectives `defines a sequence containing` CA_Perspective `enumerates.`
`Ordered set` ExposureRoutesSet
NanoFormManifestations `defines a sequence containing` NF_UseForm `enumerates.`

Operators

```
function USE_EXPOSURE_KB::EnergyLevelToStr(el :: EnergyLevel ):: String
  case el of
    el_very_high:
      result := "very high";
    el_high:
      result := "high";
    el_medium:
      result := "medium";
    el_low:
      result := "low";
    el_very_low:
      result := "very low";
    el_none:
      result := "no energy"
    else
      result := "?"
  end
```

Chapter 7 GUIDELINES_METHODS_KB



7.1 Defined enumerations

AssayDescriptor

- 'Small Angle Neutron Scattering'
  Small Angle Neutron Scattering (SANS) [ISO/TS 80004-6:2015 3.2.2]
- 'Neutron Diffraction'
  Neutron Diffraction [ISO/TS 80004-6:2015 3.2.3]
- 'Small Angle X-ray Scattering'
  Small Angle X-ray Scattering (SAXS) [ISO/TS 80004-6:2015 3.2.4]
- 'Wide-Angle X-ray Scattering'
  wide-angle X-ray scattering (WAXS) synonym wide-angle X-ray diffraction (WAXD)
- 'Dynamic Light Scattering'
  Dynamic Light Scattering (DLS), Photon Correlation Spectroscopy (PCS), Quasi-Elastic Light Scattering (QELS) [ISO/TS 80004-6:2015 3.2.7]
- 'Nanoparticle Tracking Analysis'
  Nanoparticle Tracking Analysis (NTA), Particle Tracking Analysis (PTA) [ISO/TS 80004-6:2015 3.2.8]
- 'Condensation Particle Counter'
  Condensation Particle Counter (CPC) [ISO/TS 80004-6:2015 3.3.1]
- 'Differential Electrical Mobility Classifier'
  Differential Electrical Mobility Classifier (DEMC) [ISO/TS 80004-6:2015 3.3.2]
- 'Differential Mobility Analysing System'
  Differential Mobility Analysing System (DMAS) [ISO/TS 80004-6:2015 3.3.3]
- 'ElectroSpray-Differential Mobility Analysis'
  'ElectroSpray–Differential Mobility Analysis' (ES-DMA) (also known as ElectroSpray-Scanning Mobility particle sizer (ES-SMPS))
- 'Faraday-Cup Aerosol Electrometer'
  Faraday-Cup Aerosol Electrometer (FCAE) [ISO/TS 80004-6:2015 3.3.4]
- 'Field Flow Fractionation'
  Field Flow Fractionation (FFF) [ISO/TS 80004-6:2015 3.4.1]
- 'Centrifugal Liquid Sedimentation'
  Centrifugal Liquid Sedimentation (CLS), Differential Centrifugal Sedimentation (DCS) [ISO/TS 80004-6:2015 3.4.2]
- 'Photocentrifuge'
  Photocentrifuge [ISO 13318 [6, 7]]
- 'Analytical Ultracentrifugation'
  Analytical Ultracentrifugation (AU, AUC)
- 'Size-Exclusion Chromatography '
  Size-Exclusion Chromatography (SEC) [ISO/TS 80004-6:2015 3.4.3]
- 'Electrical Zone Sensing'
  Electrical Zone Sensing, Coulter counter [ISO/TS 80004-6:2015 3.4.4]
- 'Scanning Probe Microscopy'
  Scanning Probe Microscopy (SPM) [ISO/TS 80004-6:2015 3.5.1]

- 'Atomic Force Microscopy'
  Atomic Force Microscopy (AFM) [ISO/TS 80004-6:2015 3.5.2]
- 'Scanning Tunnelling Microscopy'
  Scanning Tunnelling Microscopy (STM) [ISO/TS 80004-6:2015 3.5.3]
- 'Near-field Scanning Optical Microscopy'
  Near-field Scanning Optical Microscopy (NSOM), Scanning Near-field Optical Microscopy (SNOM) [ISO/TS 80004-6:2015 3.5.4]
- 'Scanning Electron Microscopy'
  Scanning Electron Microscopy (SEM) [ISO/TS 80004-6:2015 3.5.5]
- 'Transmission Electron Microscopy'
  Transmission Electron Microscopy (TEM) [ISO/TS 80004-6:2015 3.5.6] NPO_1430
- 'Scanning Transmission Electron Microscopy'
  Scanning Transmission Electron Microscopy (STEM) [ISO/TS 80004-6:2015 3.5.7]
- 'High-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM)'
  High-Angle Annular Dark-Field Scanning Transmission Electron Microscopy (HAADF-STEM)
- 'Low Energy Electron Microscopy'
  Low Energy Electron Microscopy (LEEM) [ISO/TS 80004-6:2015 3.5.8]
- 'Scanning Ion Microscopy'
  Scanning Ion Microscopy [ISO/TS 80004-6:2015 3.5.9]
- 'Confocal Optical Microscopy'
  Confocal Optical Microscopy [ISO/TS 80004-6:2015 3.5.10]
- 'Surface Enhanced Ellipsometric Contrast Microscopy'
  Surface Enhanced Ellipsometric Contrast Microscopy (SEEC microscopy) [ISO/TS 80004-6:2015 3.5.11]
- 'Fluorescence Microscopy'
  Fluorescence Microscopy [ISO/TS 80004-6:2015 3.5.13]
- 'Total Internal Reflection Fluorescence Microscopy'
  Total Internal Reflection Fluorescence Microscopy (TIRF microscopy) [ISO/TS 80004-6:2015 3.5.14]
- 'Super-Resolution Microscopy'
  Super-Resolution Microscopy [ISO/TS 80004-6:2015 3.5.15]
- 'Localization Microscopy'
  Localization Microscopy [ISO/TS 80004-6:2015 3.5.16]
- 'Brunauer-Emmett-Teller method'
  Brunauer–Emmett–Teller method (BET method) [ISO/TS 80004-6:2015 3.6.3]
- 'Volumetric Centrifugation Method'
  Volumetric Centrifugation Method (VCM) (used for determination of effective density) [ISO 18747-1:2018(en)] Volumetric Cell Measurement (VCM) Is this the same?? NANOREG DISPERSION PROTOCOL, VOLUMETRIC CELL MEASURMENT (VCM), ADAPTED FROM DELOID ET AL 2014, 2017
- 'Photoluminescence Spectroscopy'
  Photoluminescence Spectroscopy (PL spectroscopy) [ISO/TS 80004-6:2015 4.4]
- 'Fluorescence Spectroscopy'
  Fluorescence Spectroscopy [ISO/TS 80004-6:2015 4.5]
- 'UV-Vis spectroscopy'
  UV–Vis spectroscopy [ISO/TS 80004-6:2015 4.6]
- 'Fluorescence Correlation Spectroscopy'
  Fluorescence Correlation Spectroscopy [ISO/TS 80004-6:2015 4.7]
- 'Fourier Transform Infrared Spectroscopy'
  Fourier Transform Infrared Spectroscopy (FTIR) [ISO/TS 80004-6:2015 4.8]
- 'Raman Spectroscopy'
  Raman spectroscopy [ISO/TS 80004-6:2015 4.10]
- 'Surface Enhanced Raman Spectroscopy'
  Surface Enhanced Raman Spectroscopy (SERS) [ISO/TS 80004-6:2015 4.11]
- 'Tip Enhanced Raman Spectroscopy'
  Tip Enhanced Raman Spectroscopy (TERS) [ISO/TS 80004-6:2015 4.12]
- 'Electron Energy Loss Spectroscopy'
  Electron Energy Loss Spectroscopy (EELS) [ISO/TS 80004-6:2015 4.14]
- 'Auger Electron Spectroscopy'
  Auger Electron Spectroscopy (AES) [ISO/TS 80004-6:2015 4.16]
- 'Ultraviolet Photoelectron Spectroscopy'
  Ultraviolet Photoelectron Spectroscopy (UPS) [ISO/TS 80004-6:2015 4.17]
- 'X-ray Photoelectron Spectroscopy'
  X-ray Photoelectron Spectroscopy (XPS) [ISO/TS 80004-6:2015 4.18]
- 'X-ray Absorption Spectroscopy'
  X-ray Absorption Spectroscopy (XAS) [ISO/TS 80004-6:2015 4.19]
- 'X-Ray Fluorescence'
  X-Ray Fluorescence (XRF) [ISO/TS 80004-6:2015 4.20] (not sure if just definition or actual type of measurement)
- 'Energy-Dispersive X-ray Spectroscopy'
  Energy-Dispersive X-ray Spectroscopy (EDS)/(EDX) [ISO/TS 80004-6:2015 4.21]

- 'Inductively Coupled Plasma Mass Spectrometry'
  Inductively Coupled Plasma Mass Spectrometry (ICP-MS) [ISO/TS 80004-6:2015 4.22] CHMO:0000538
- 'Single Particle Inductively Coupled Plasma Mass Spectrometry'
  Single Particle Inductively Coupled Plasma Mass Spectrometry (SP-ICP-MS)
- 'Inductively Coupled Plasma Optical Emission Spectrometry'
  Inductively Coupled Plasma - Optical Emission Spectrometry (ICP-OES) [??] also referred to as (ICP-AES) Inductivly coupled plasma atomic emission spectroscopy [NANoREG D2.08 SOP 06]
- 'Secondary-Ion Mass Spectrometry'
  Secondary-Ion Mass Spectrometry (SIMS) [ISO/TS 80004-6:2015 4.23]
- 'Atom-Probe Tomography'
  Atom-Probe Tomography [ISO/TS 80004-6:2015 4.24]
- 'Evolved-Gas Analysis'
  Evolved-Gas Analysis (EGA) [ISO/TS 80004-6:2015 4.25]
- 'Nuclear Magnetic Resonance Spectroscopy'
  Nuclear Magnetic Resonance Spectroscopy (NMR spectroscopy) [ISO/TS 80004-6:2015 4.26]
- 'Electron Paramagnetic Resonance'
  Electron Paramagnetic Resonance (EPR), Electron Spin Resonance (ESR) [ISO/TS 80004-6:2015 4.27]
- 'Mössbauer Spectroscopy'
  Mössbauer Spectroscopy [ISO/TS 80004-6:2015 4.28]
- 'Dual Polarization Interferometry'
  Dual Polarization Interferometry (DPI) [ISO/TS 80004-6:2015 4.29]
- 'Quartz Crystal Microbalance'
  Quartz Crystal Microbalance (QCM) [ISO/TS 80004-6:2015 5.1.1]
- 'Thermogravimetry'
  Thermogravimetry (TG), Thermo Gravimetic Analysis (TGA) [ISO/TS 80004-6:2015 5.1.1]
- 'Thermogravimetric Analysis/Mass Spectrometry'
  Thermogravimetric Analysis/Mass Spectrometry (TGA-MS)
- 'Differential Scanning Calorimetry'
  Differential Scanning Calorimetry (DSC) [ISO/TS 80004-6:2015 5.1.3]
- 'X-ray diffraction'
  X-Ray Diffraction (XRD) [ISO/TS 80004-6:2015 5.2.1]
- 'Electron BackScatter Diffraction'
  Electron BackScatter Diffraction (EBSD) [ISO/TS 80004-6:2015 5.2.2]
- 'Selected Area Electron Diffraction'
  'Selected Area Electron Diffraction' (SAED) isn't this the same as Electron Backscatter Diffraction??
- 'Sears titration'
  Sears titration used for Specific Surface Area
- 'Drop shape analysis'
  Drop shape analysis (DSA) The contact angle is measured using the image of a sessile drop at the points of intersection (three-phase contact points) between the drop contour and the projection of the surface (baseline).
- 'Wilhelmy plate method'
  The force acting in the tensile direction when moving a plate-shaped solid vertically in a liquid is measured. This force depends on the contact angle as well as on the surface tension and the wetted length.
- 'Washburn method'
  Powder contact angle measurement using the Washburn method: The increase in weight of an immersed powder-filled tube is measured with respect to time. The rate of rise of the liquid column depends, among other things, on the contact angle.
- 'Top-view distance method'
  The curvature of the drop surface associated with the contact angle is measured using the distance between light spots which are reflected on the top of a drop surface.
- 'CHN-Analysis'
  The determination of Carbon, Hydrogen and Nitrogen content.
- 'Zero-field cooled/field cooled curves'
  Zero-field cooled/field cooled curves (used to determine magnetic behaviour)
- 'Vortex Shaker'
  Vortex Shaker (VS) method, (used to determine dustiness)
- 'Small rotating Drum'
  Small rotating Drum method (used to determine dustiness)
- 'Vibro Fluidization'
  Vibro Fluidization method, (used to determine dustiness)
- 'Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy'
  Attenuated Total reflectance Fourier transform infrared spectroscopy (ATR-FTIR)
- 'Helium pycnometry'
  Helium pycnometry (HE-pycnometry) [ISO 21687]
- 'Ferric Reduction Ability of Serum'
  Ferric Reduction Ability of Serum (FRAS) (see WP D5.3) (acellular tests)
- 'Dichlorodihydrofluorescin diacetate'
  Dichlorodihydrofluorescin diacetate (DCFH) (see WP D5.3) Is this the same as DCFH2-DA assay (see D5.5 5.6 5.7 Deliverable) acellular tests
- 'Rhodamine-B dye degradation'
  Rhodamine-B dye degradation (see WP5 D5.3) (Photoreactivity)

- 'Diffusion-Ordered Spectroscopy with Nuclear Magnetic Resonance'
  Diffusion-Ordered Spectroscopy with Nuclear Magnetic Resonance (DOSYNMR) (see ENV-JM-MONO(2016)7)
- 'Laser Doppler Electrophoresis'
  Laser Doppler Electrophoresis (LDE)??
- 'Electrophoretic Light Scattering'
  Electrophoretic light scattering (ELS) (ISO 13099-2:2012) (Zeta potential, surface charge) http://purl.obolibrary.org/obo/CHMO_0001826
- 'Multiple Path Particle Dosimetry model'
  Multiple Path Particle Dosimetry model (MPPD)
- 'Static dissolution system'
  Screening dissolution test, according to OECD TG on Dissolution (Project 3.10, latest draft May 2018). Static dissolution system (ISO 19057:2017) 10.5.2
- 'Continuous Flow System'
  Continuous Flow System (CFS) (ISO 19057:2017) 10.5.3, OECD GD (ENV/JM/MONO(2020)9- TG for NM dissolution in preparation
- 'In Vivo Mammalian Alkaline COMET Assay'
  In Vivo Mammalian Alkaline Comet .. Test No. 489:
- 'Cascade in vitro digestion Assay'
  NANoREG D2.08 SOP 06
- 'Ultrafiltration'
  UF
- 'Ultrafiltration – Inductivly Coupled Plasma Atomic Emission Spectroscopy'
  'Ultrafiltration - Inductivly Coupled Plasma Atomic Emission Spectroscopy' (UF-ICP/AES) (combination of UF and ICP/AES)
- 'Cell Profiliration Assay'
- 'Lactate DeHydrogenase Assay'
  Lactate dehydrogenase assay (LDH), LDH cytotoxicity assay (Measures cell membrane integrity) LDH release assay NPO_1709
- 'Alamar Blue Metabolic Cell Viability Assay'
- 'WST-1 Metabolic Cell Viability Assay'
- 'WST-8 Metabolic Cell Viability Assay'
- 'Embryonic Stem Cell Test'
  Embryonic Stem Cell Test (EST)
- 'Neutral Red Uptake Cell Viability Assay'
  Neutral red uptake assay (NRU)
- 'Resazurin Metabolic Cell Viability Assay'
- 'Colony Forming Efficiency Assay'
  Colony Forming Efficiency Assay (CFE) (cytotoxicity assay)
- 'TransEpithelial Electrical Resistance Assay'
  Transepithelial electrical resistance (TEER)
- 'Enzyme-Linked Immunosorbent Assay'
  enzyme-linked immunosorbent assay, (ELISA)
- 'Cascade Impactor Measurement'
  Cascade Impactor Measurement ()
- 'Screening dispersion Assay'
  Batch stability assay (OECD TG 318) => Screening dispersion test
- 'Screening heteroaggregation dispersion Assay '
- 'Screening batch retention Test'
  NanoFASE1 (based on OECD 106)
- 'Extended dispersion Assay'
  Batch stability assay (OECD TG 318) => Extended dispersion test
- 'Biodegradation MT-2 screening Assay'
  Biodegradation MT2 screening in activated sludge (GRACIOUS MT2 SOP under development) E-G-4a
- 'Biodegradation DOC Die-Away Assay'
  Biodegradation DOC Die-Away Assay [OECD 301-A]
- 'Biodegradation CO2 Evolution Assay'
  Biodegradation CO2 evolution (E-G-4) [OECD 301-B]
- 'Biodegradation MITI (I) Assay'
  Biodegradation MITI (I) [OECD 301-C]
- 'Biodegradation Closed Bottle Assay'
  Biodegradation Closed Bottle E-G-4 [OECD 301-E]
- 'Biodegradation Modified OECD screening Assay'
  Biodegradation modified OECD screening E-G-4 [OECD 301-D]
- 'Biodegradation Manometric Respirometry Assay'
  Biodegradation Manometric Respirometry E-G-4 [OECD 301-F, ISO 14851 2019]
- 'Biodegradation Aerobic sewage Assay'
  Biodegradation Aerobic sewage E-G-4 [OECD 303]
- 'Biodegradation wastewater discharge, sewer systems Assay'
  Biodegradability of Chemicals Discharged in Wastewater, sewer systems E-G-4 [OECD 314-A]

- 'Biodegradation wastewater discharge, activated sludge Assay'
  Biodegradability of Chemicals Discharged in Wastewater, activated sludge E-G-4 [OECD 314-B]
- 'Biodegradation wastewater discharge, anaerobic digester sludge'
  Biodegradability of Chemicals Discharged in Wastewater, anaerobic digester sludge E-G-4 [OECD 314-C]
- 'Biodegradation wastewater discharge, treated effluent in the mixing zone of surface water'
  Biodegradability of Chemicals Discharged in Wastewater, treated effluent in the mixing zone of surface water E-G-4 [OECD 314-D]
- 'Biodegradation wastewater discharge, untreated wastewater that is directly discharged to surface water'
  Biodegradability of Chemicals Discharged in Wastewater, untreated wastewater that is directly discharged to surface water E-G-4 [OECD 314-E]
- 'Macrophage-assisted dissolution Assay'
  Macrophage-assisted dissolution assay
- 'In vitro biological stiffness Assay'
  In vitro biological stiffness assay, (Zhu et al in situ assessment of rigidity by TEM after NF uptake by macrophages) In vitro rigidity Assay, In vitro incuabiton with macrophages, fibre size measurements in situ by TEM
- 'In vivo rigidity Assay'
  In vivo rigidity Assay, Mophological assessment of fibres in lung section slices, Mercer et al
- 'Buckling Criterion Model'
  Buckling Criterion model, Calculated threshold for HARN buckling under a typical compressive force exerted by the lysosomal membrane (20pN). Zhu et al 2016
- 'Inflammasome activation'
  Inflammasome activation
- 'Durability in cellular systems'
  Assay based on protocol from Kolterman Jully et al 2018 (no validated SOP) (H-I-1)
- 'In vivo intratracheal instillation Assay'
  Provide information (OECD GD 39) => Not to be used for Risk Assessment
- 'Short Term Inhalation Study'
  Short Term Inhalation Study (STIS)
- 'Subacute Inhalation Toxicity Assay'
  Subacute Inhalation Toxicity Assay (OECD 412) In vivo inhalation study
- 'Subchronic Inhalation Toxicity Assay'
  Subchronic Inhalation Toxicity Assay (OECD 413) In vivo inhalation study
- 'Nanomaterial removal in wastewater Assay'
  OECD WNT 3.11
- 'Direct photolysis theroretical screening Assay'
  Direct photolysis theroretical screening (OECD 316)
- 'Inherent biodegradability in soil Assay'
  Inherent biodegradability in soil (304-A)
- 'Photodegradation at soil surface Assay'
  Photodegradation at soil surface (EPA GSD N 161-3)
- 'Aerobic soil transformation Assay'
  Aerobic soil transformation (OECD 307)
- 'DLVO attachment efficiency derivation method'
  DLVO attachment efficiency derivation (SimpleBox4nano)
- 'Lipid Peroxidation (MDA) Assay'
  Lipid Peroxidation (MDA) Assay
- 'DAN fluorimetric Assay'
  DAN fluorimetric Assay
- 'Cytokinesis Block Micronucleus Cytome Assay'
  Cytokinesis Block Micronucleus Cytome (CBMN Cyt) Assay
- 'MTT Cell Viability Assay'
- 'MTS Cell Viability Assay'
  MTS assay is a colorimetric method for sensitive quantification of viable cells in cell proliferation assay.
- 'Glutathione Assay'
  Glutathione Assay (GSH)
- 'Haemolysis Assay'
- 'Calcein-Ethidium Assay'
- 'Cell Transformation Assay'
  Cell Transformation Assay (CTA)
- 'Griess Reagent Assay'
  The Griess test is an analytical chemistry test which detects the presence of nitrite ion in solution. ENM_8000278
- 'Lucifer Yellow Assay'
  Lucifer Yellow assay for determination of the epithelial barrier function.
- 'Impedance Analysis of Adherent Cells'
- 'Impedance Flow Cytometry'
  IMPEDANCE FLOW CYTOMETRY (IFC)
- 'Filtration ICP-MS'
  'Filtration ICP-MS' ENM_8000258

- 'Potentiometry Assay'
  Potentiometry assay (pH measurement)
- 'Reverse transcription polymerase chain reaction'
  Reverse transcription polymerase chain reaction (RT-PCR) OBI_0001170
- 'In vitro alveolar macrophage Assay'
  in vitro NR8383 alveolar macrophage assay
- 'In vitro granuloma formation Assay'
- 'Screening transformation/dissolution test – sparingly soluble metal compounds'
  Screening transformation/dissolution test – sparingly soluble metal compounds (OECD 29)
- 'Full transformation/dissolution test - metals and sparingly soluble metal compounds'
  Full transformation/dissolution test - metals and sparingly soluble metal compounds (OECD 29)
- 'Protein Carbonylation Assay'
  Protein Carbonylation Assay (Oxiblot kit (Millipore)
- 'Freshwater Alga and Cyanobacteria, Growth Inhibition Test'
  Freshwater Alga and Cyanobacteria, Growth Inhibition Test (OECD 201)
- 'Daphnia sp. Acute Immobilisation Test'
  Daphnia sp. Acute Immobilisation Test (OECD 202)
- 'Batch dispersion quality Assay'
  https://www.rivm.nl/sites/default/files/2018-11/NANoREG_Guidance_Document.pdf
- 'Repeated Dose 90-Day Oral Toxicity Study in Rodents'
  Repeated Dose 90-Day Oral Toxicity Study in Rodents (OECD TG 408)
- 'Consecutive in vitro digestion Assay'
  Trace the NM fate (in term of dissolution and size) using simulated human digestive fluids (NANoREG D2.08 SOP 06)
- 'NRF2 Activation Assay'
  SOP reference: GRACIOUS-TMDF-InVitro-WP5-P8-inVitro-Nrf2activation.doc
- 'Short Term Screening 21-day Fish Assay'
  21-day Fish Assay: A Short Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition (OECD 230)
- 'Water Solubility Assay'
  Water Solubility Test (OECD 105)
- 'Microtox assay'
  Microtox assay (Vibrio fischeri) [Environment Canada (2002) EPS 1/RM/42]
- 'Caenorhabditis elegans sediment toxicity test'
  Water and soil quality – Determination of the toxic effect of sediment and soil samples on growth, fertility and reproduction of Caenorhabditis elegans
- 'Water-sediment Myriophyllum spicantum toxicity test'
  Water-sediment Myriophyllum spicantum toxicity test [OECD 239]
- 'Sediment-water Lumbriculus toxicity test using spiked sediment'
  Sediment-water Lumbriculus toxicity test using spiked sediment [OECD 225]
- 'Sediment-water Chironomid spiked sediment toxicity test'
- 'Leptocherius plumulosus chronic marine and estuarine sediment toxicity test'
- 'Simulated freshwater lentic field test'
  Simulated freshwater lentic field tests (outdoor microcosm and mesocosms) [OECD 53]
- 'Fish, Early-life Stage Toxicity Test'
  Fish, Early-life Stage Toxicity Test [OECD 210]
- 'Fish embryo acute toxicity (FET) test'
  'Fish embryo acute toxicity (FET) test' [OECD 236]
- 'Daphnia magna Reproduction Test'
- 'LUMINEX Assay'
- 'CFDA-AM Assay'
  CFDA-AM
- 'Isothermal Titration Calorimetry Assay'
  Isothermal Titration Calorimetry (ITC)
- 'In Vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes'
  OECD 476
- 'In Vitro Mammalian Cell Gene Mutation Tests using the Thymidine Kinase Gene'
  OECD 490
- 'In Vitro Mammalian Chromosomal Aberration Test'
  OECD 473
- 'In Vitro Mammalian Cell Micronucleus Test'
  (MNvit) OECD 487
- 'Transgenic Rodent Somatic and Germ Cell'
  OECD 488
- 'May-Grunwald Giemsa coloration of BAL cells cytospin'
  NanoReg..
- 'In vivo oral toxicokinetic Study'
  In vivo toxicokinetic study [OECD 417]

- 'Column leaching Test'
  Column leaching test [OECD 312] WNT Project 3.14: Guidance Document to support the use of TG312 (Leaching in soil columns)
- 'Tunable Resistive Pulse Sensing'
  Tunable resistive pulse sensing (TRPS)
- 'Heme Oxygenase 1 Assay'
  heme oxygenase 1 oxidative stress assay (HMOX)
  Heme oxygenases have been characterized as markers for oxidative stress, metabolic disorders and inflammation. Heme oxygenase 1 is induced in the bloodstream by oxidative stress.
- 'Microbiota cell wall integrity Assay'
  Assay to qualify the damage/integrity of bacterial cell wall. (Gracious ORAL IATAs)

ISO

International Organization for Standardization

- 'ISO 60'
  ISO 60 (Plastics – Determination of apparent density of material that can be poured from a specific funnel) [58573]
- 'ISO 787-11'
  General methods of test for pigments and extenders – Part 11: Determination of tamped volume and apparent density after tamping [58574]
- 'ISO 2431'
  Paints and varnishes - Determination of flow time by use of flow cups [60162]
- 'ISO 3104'
  Petroleum products - Transparent and opaque liquids - Determination of kinematic viscosity and calculation of dynamic viscosity [60163]
- 'ISO 3105'
  Glass capillary kinematic viscometers - Specifications and operating instructions [60164]
- 'ISO 3219'
  Plastics; polymers/resins in the liquid state or as emulsions or dispersions; determination of viscosity using a rotational viscometer with defined shear rate [60165]
- 'ISO DP 6060'
  Water Quality - Determination of the Chemical Oxygen Demand [880]
- 'ISO 5815'
  Water quality - Determination of Biochemical Oxygen Demand after 5 Days (BOD5) - Dilution and Seeding Method [868]
- 'ISO 6341'
  Water quality - Determination of the Inhibition of the Mobility of Daphnia magna Straus (Cladocera, Crustacea) [869]
- 'ISO 7827'
  Evaluation in an Aqueous Medium of the "Ultimate" Aerobic Biodegradability of Organic Compounds - Method by Analysis of Dissolved Organic Carbon (DOC) [874]
- 'ISO 7346-1'
  Determination of the Acute Lethal Toxicity of Substances to a Freshwater Fish [Brachydanio rerio Hamilton-Buchanan (Teleostei, Cyprinidae)] - Part 1: Static Method [870]
- 'ISO 7346-2'
  Determination of the Acute Lethal Toxicity of Substances to a Freshwater Fish [Brachydanio rerio Hamilton-Buchanan (Teleostei, Cyprinidae)] - Part 2: Semi-static method [871]
- 'ISO 7346-3'
  Determination of the Acute Lethal Toxicity of Substances to a Freshwater Fish [Brachydanio rerio Hamilton-Buchanan (Teleostei, Cyprinidae)] - Part 3: Flow-through method [872]
- 'ISO 8192'
  Water quality - Test for inhibition of oxygen consumption by activated sludge for carbonaceous and ammonium oxidation [875]
- 'ISO 8692'
  Water Quality - Fresh Water Algal Growth Inhibition Test with Scenedesmus subspicatus and Selenastrum capricornutum [876]
- 'ISO 9277'
  Determination of the specific surface area of solids by gas adsorption - BET method [58539]
- 'ISO DIS 9408'
  Ultimate Aerobic Biodegradability - Method by Determining the Oxygen Demand in a Closed Respirometer [877]
- 'ISO DIS 9439'
  Ultimate Aerobic Biodegradability - Method by Analysis of Released Carbon Dioxide [878]
- 'ISO 9509'
  Toxicity test for assessing the inhibition of nitrification of activated sludge microorganisms [879]
- 'ISO 9887 '
  Water quality - Evaluation of the aerobic biodegradability of organic compounds in an aqueous medium - Semi-continuous activated sludge method (SCAS) [60760]
- 'ISO 9888'
  Water quality - Evaluation of ultimate aerobic biodegradability of organic compounds in aqueous medium - Static test (Zahn-Wellens method) [60761]
- 'ISO 10253'
  ISO 10253 (Water quality - Marine Algal Growth Inhibition Test with Skeletonema costatum and Phaeodactylum tricornutum) [861]
- 'ISO 10707'
  Water quality - Evaluation in an aqueous medium of the "ultimate" aerobic biodegradability of organic compounds - Method by analysis of biochemical oxygen demand (closed bottle test) [60762]
- 'ISO 10708'
  Water quality - Evaluation in an aqueous medium of the ultimate aerobic biodegradability of organic compounds - Determination of biochemical oxygen demand in a two-phase closed bottle test [60763]
- 'ISO 10712'
  Water quality – Pseudomonas putida growth inhibition test (Pseudomonas cell multiplication inhibition test) [60851]

- 'ISO/TS 10797:2012'
  ISO/TS 10797:2012 Nanotechnologies – Characterization of single-wall carbon nanotubes using transmission electron microscopy
- 'ISO/TS 10798:2011'
  ISO/TS 10798:2011 Nanotechnologies – Charaterization of single-wall carbon nanotubes using scanning electron microscopy and energy dispersive X-ray spectrometry analysis
- 'ISO 10801:2010'
  ISO 10801:2010 Nanotechnologies – Generation of metal nanoparticles for inhalation toxicity testing using the evaporation/condensation method
- 'ISO 10808:2010'
  ISO 10808:2010 Nanotechnologies – Characterization of nanoparticles in inhalation exposure chambers for inhalation toxicity testing
- 'ISO/TS 10867:2010'
  ISO/TS 10867:2010 Nanotechnologies – Characterization of single-wall carbon nanotubes using near infrared photoluminescence spectroscopy
- 'ISO/TS 10868:2017 '
  ISO/TS 10868:2017 Nanotechnologies – Characterization of single-wall carbon nanotubes using ultraviolet-visible-near infrared (UV-Vis-NIR) absorption spectroscopy
- 'ISO 10872:2020'
  ISO 10872:2020 - Water and soil quality – Determination of the toxic effect of sediment and soil samples on growth, fertility and reproduction of Caenorhabditis elegans
- 'ISO/TR 10929:2012'
  ISO/TR 10929:2012 Nanotechnologies – Characterization of multiwall carbon nanotube (MWCNT) samples
- 'ISO/TS 11251:2019'
  ISO/TS 11251:2019 Nanotechnologies – Characterization of volatile components in single-wall carbon nanotube samples using evolved gas analysis/gas chromatograph-mass spectrometry
- 'ISO 11267'
  Inhibition of Reproduction of Collembola by Soil Pollutants [862]
- 'ISO 11268-1'
  Effects of Pollutants on Earthworms. 1. Determination of Acute Toxicity Using Artificial Soil Substrate [863]
- 'ISO 11268-2'
  Effects of Pollutants on Earthworms. 2. Determination of Effects on Reproduction [864]
- 'ISO 11268-3'
  Effects of Pollutants on Earthworms. 3. Guidance on the Determination of Effects in Field Situations [865]
- 'ISO 11269-1'
  Soil quality - Determination of the effects of pollutants on soil flora - Part 1: Method for the measurement of inhibition of root growth [61196]
- 'ISO 11269-2'
  Soil quality - Determination of the effects of pollutants on soil flora - Part 2: Effects of contaminated soil on the emergence and early growth of higher plants [61197]
- 'ISO/TS 11308:2011'
  ISO/TS 11308:2011 Nanotechnologies – Characterization of single-wall carbon nanotubes using thermogravimetric analysis
- 'ISO/TR 11360:2010'
  ISO/TR 11360:2010 Nanotechnologies – Methodology for the classification and categorization of nanomaterials
- 'ISO 11733'
  Water quality - Determination of the elimination and biodegradability of organic compounds in an aqueous medium - Activated sludge simulation test [61252]
- 'ISO 11734'
  Water quality - Evaluation of the ”ultimate” anaerobic biodegradability of organic compounds in digested sludge - Method by measurement of the biogas production [60764, 61253]
- 'ISO/TR 11811:2012'
  ISO/TR 11811:2012 Nanotechnologies – Guidance on methods for nano- and microtribology measurements
- 'ISO/TS 11888:2017'
  ISO/TS 11888:2017 Nanotechnologies — Characterization of multiwall carbon nanotubes — Mesoscopic shape factors
- 'ISO/TS 11931:2012'
  ISO/TS 11931:2012 Nanotechnologies – Nanoscale calcium carbonate in powder form – Characteristics and measurement
- 'ISO/TS 11937:2012'
  ISO/TS 11937:2012 Nanotechnologies – Nanoscale titanium dioxide in powder form – Characteristics and measurement
- 'ISO/TS 12025:2012'
  ISO/TS 12025:2012 Nanomaterials – Quantification of nano-object release from powders by generation of aerosols
- 'ISO 12058-1'
  ISO 12058-1 Plastics - Determination of viscosity using a falling-ball viscometer - Part 1: Inclined-tube method [60161]
- 'ISO/TR 12802:2010'
  ISO/TR 12802:2010 Nanotechnologies – Model taxonomic framework for use in developing vocabularies – Core concepts
- 'ISO/TS 12805:2011'
  ISO/TS 12805:2011 Nanotechnologies – Materials specifications – Guidance on specifying nano-objects
- 'ISO/TR 12885:2018'
  ISO/TR 12885:2018 Nanotechnologies – Health and safety practices in occupational settings
- 'ISO/TS 12901-1:2012'
  ISO/TS 12901-1:2012 Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 1: Principles and approaches
- 'ISO/TS 12901-2:2014'
  ISO/TS 12901-2:2014 Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 2: Use of the control banding approach
- 'ISO/TR 13014:2012'
  ISO/TR 13014:2012 Nanotechnologies - Guidance on physicochemical characterization of engineered nanoscale materials for toxicologic assessment

- 'ISO/TR 13121:2011'
  ISO/TR 13121:2011 Nanotechnologies – Nanomaterial risk evaluation
- 'ISO/TS 13278:2017'
  ISO/TS 13278:2017 Nanotechnologies – Determination of elemental impurities in samples of carbon nanotubes using inductively coupled plasma mass spectrometry
- 'ISO/TR 13329:2012'
  ISO/TR 13329:2012 Nanomaterials – Preparation of material safety data sheet (MSDS)
- 'ISO/TS 13830:2013'
  ISO/TS 13830:2013 Nanotechnologies – Guidance on voluntary labelling for consumer products containing manufactured nano-objects
- 'ISO 13318-2'
  Determination of particle size distribution by centrifugal liquid sedimentation methods - Part 2: Photocentrifuge method [60081]
- 'ISO 13320'
  Particle size analysis - Laser diffraction methods [60082]
- 'ISO 13641-1'
  Determination of inhibition of gas production of anaerobic bacteria – Part 1:General test [60852]
- 'ISO 13641-2'
  Determination of inhibition of gas production of anaerobic bacteria – Part 2:Test for low biomass concentrations [60853]
- 'ISO/TS 14101:2012'
  ISO/TS 14101:2012 Surface characterization of gold nanoparticles for nanomaterial specific toxicity screening: FT-IR method
- 'ISO 14238'
  [866]
- 'ISO 14593:1999'
  Water quality - Evaluation of ultimate aerobic biodegradability of organic compounds in aqueous medium - Method by analysis of inorganic carbon in sealed vessels (CO2 headspace test) [60765]
- 'ISO 14592-1'
  Water quality - Evaluation of the aerobic biodegradability of organic compounds at low concentrations - Part 1: Shake-flask batch test with surface water or surface water/sediment suspensions [61254]
- 'ISO 14592-2'
  Water quality - Evaluation of the aerobic biodegradability of organic compounds at low concentrations - Part 2: Continuous flow river model with attached biomass [61255]
- 'ISO/TR 14786:2014'
  ISO/TR 14786:2014 Nanotechnologies – Considerations for the development of chemical nomenclature for selected nano-objects
- 'ISO 14851:2019'
  Determination of the ultimate aerobic biodegradability of plastic materials in an aqueous medium — Method by measuring the oxygen demand in a closed respirometer
- 'ISO 15522'
  Water quality - Determination of the inhibitory effect of water constituents on the growth of activated sludge microorganisms [60854]
- 'ISO 15901-1'
  Pore size distribution and porosity of solid materials by mercury porosimetry and gas adsorption - Part 1: Mercury porosimetry [58566]
- 'ISO 15901-2'
  Pore size distribution and porosity of solid materials by mercury porosimetry and gas adsorption – Part 2: Analysis of mesopores and macropores by gas adsorption [58567]
- 'ISO 15901-3'
  Pore size distribution and porosity of solid materials by mercury porosimetry and gas adsorption – Part 3: Analysis of micropores by gas adsorption
- 'ISO DIS 17556.2'
  Plastics - Determination of the Ultimate Aerobic Biodegradability in Soil by Measuring the Oxygen Demand in a Respirometer or the Amount of Carbon Dioxide Evolved [1]
- 'ISO 21501-2'
  Determination of particle size distribution - Single particle light interaction methods - Part 2: Light scattering liquid-borne particle counter [60083]
- 'ISO 21501-3'
  Determination of particle size distribution - Single particle light interaction methods - Part 3: Light extinction liquid-borne particle counter [60266]
- 'ISO/TS 16195:2018'
  ISO/TS 16195:2018 Nanotechnologies – Specification for developing representative test materials consisting of nano-objects in dry powder form
- 'ISO/TR 16196:2016'
  ISO/TR 16196:2016 Nanotechnologies – Compilation and description of sample preparation and dosing methods for engineered and manufactured nanomaterials
- 'ISO/TR 16197:2014'
  ISO/TR 16197:2014 Nanotechnologies – Compilation and description of toxicological and ecotoxicological screening methods for engineered and manufactured nanomaterials
- 'ISO/TS 16550:2014'
  ISO/TS 16550:2014 Nanoparticles - Determination of muramic acid as a biomarker for silver nanoparticles activity
- 'ISO 16387'
  [867]
- 'ISO 17126'
  Soil quality - Determination of the effects of pollutants on soil flora - Screening test for emergence of lettuce seedlings (Lactuca sativa L.) [61198]
- 'ISO/TS 17200:2020'
  ISO/TS 17200:2013 Nanotechnologies – Nanoparticles in powder form – Characteristics and measurements
- 'ISO/TR 17302:2015'
  ISO/TR 17302:2015 Nanotechnologies – Framework for identifying vocabulary development for nanotechnology applications in human healthcare
- 'ISO/TS 17466:2015'
  ISO/TS 17466:2015 Use of UV-Vis absorption spectroscopy in the characterization of cadmium chalcogenide colloidal quantum dots
- 'ISO/TS 18110:2015'
  ISO/TS 18110:2015 Nanotechnologies – Vocabularies for science, technology and innovation indicators

- 'ISO/TR 18196:2016'
  ISO/TR 18196:2016 Nanotechnologies – Measurement technique matrix for the characterization of nano-objects
- 'ISO/TR 18401:2017'
  ISO/TR 18401:2017 Nanotechnologies – Plain language explanation of selected terms from the ISO/IEC 80004 series
- 'ISO/TR 18637:2016'
  ISO/TR 18637:2016 Nanotechnologies – Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs)
- 'ISO/TS 18827:2017'
  ISO/TS 18827:2017 Nanotechnologies – Electron spin resonance (ESR) as a method for measuring reactive oxygen species (ROS) generated by metal oxide nanomaterials
- 'ISO/TS 19006:2016'
  ISO/TS 19006:2016 Nanotechnologies – 5-(and 6)-Chloromethyl-2¿,7¿ Dichloro-dihydrofluorescein diacetate (CM-H2DCF-DA) assay for evaluating nanoparticleinduced intracellular reactive oxygen species (ROS) production in RAW 264.7 macrophage cell line
- 'ISO 19007:2018'
  ISO 19007:2018 Nanotechnologies – In vitro MTS assay for measuring the cytotoxic effect of nanoparticles
- 'ISO 19057:2017'
  ISO/TR 19057:2017 Nanotechnologies – Use and application of acellular in vitro tests and methodologies to assess nanomaterial biodurability
- 'ISO/TS 19337:2016'
  ISO/TS 19337:2016 Nanotechnologies – Characteristics of working suspensions of nano-objects for in vitro assays to evaluate inherent nano-object toxicity
- 'ISO/TS 19590:2017'
  ISO/TS 19590:2017 Nanotechnologies – Size distribution and concentration of inorganic nanoparticles in aqueous media via single particle inductively coupled plasma mass spectrometry
- 'ISO/TR 19601:2017'
  ISO/TR 19601:2017 Nanotechnologies – Aerosol generation for air exposure studies of nano-objects and their aggregates and agglomerates (NOAA)
- 'ISO/TR 19716:2016'
  ISO/TR 19716:2016 Nanotechnologies – Characterization of cellulose nanocrystals
- 'ISO/TR 19733:2019'
  ISO/TR 19733:2019 Nanotechnologies – Matrix of properties and measurement techniques for graphene and related two-dimensional (2D) materials
- 'ISO/TS 19807-1:2019'
  ISO/TS 19807-1:2019 Nanotechnologies — Magnetic nanomaterials — Part 1: Specification of characteristics and measurements for magnetic nanosuspensions
- 'ISO/TS 20477:2017'
  ISO/TS 20477:2017 Nanotechnologies – Standard terms and their definition for cellulose nanomaterial
- 'ISO/TR 20489:2018'
  ISO/TR 20489:2018 Nanotechnologies – Sample preparation for the characterization of metal and metal-oxide nano-objects in water samples
- 'ISO/TS 20660:2019'
  ISO/TS 20660:2019 Nanotechnologies — Antibacterial silver nanoparticles — Specification of characteristics and measurement methods
- 'ISO/TS 20787:2017'
  ISO/TS 20787:2017 Nanotechnologies - Aquatic toxicity assessment of manufactured nanomaterials in saltwater lakes using Artemia sp. Nauplii
- 'ISO/TS 21236-1:2019'
  ISO/TS 21236-1:2019 Nanotechnologies — Clay nanomaterials — Part 1: Specification of characteristics and measurement methods for layered clay nanomaterials
- 'ISO/TS 21361:2019'
  ISO/TS 21361:2019 Nanotechnologies – Method to quantify air concentrations of carbon black and amorphous silica in the nanoparticle size range in a mixed dust manufacturing environment
- 'ISO/TS 21362:2018'
  ISO/TS 21362:2018 Nanotechnologies – Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation
- 'ISO/TR 21386:2019'
  ISO/TR 21386:2019 Nanotechnologies – Considerations for the measurement of nano-objects and their aggregates and agglomerates (NOAA) in environmental matrices
- 'ISO/TR 22019:2019'
  ISO/TR 22019:2019 Nanotechnologies — Considerations for performing toxicokinetic studies with nanomaterials
- 'ISO 22030'
  Soil quality - Biological methods - Chronic toxicity in higher plants [61199]
- 'ISO 29701:2010'
  ISO 29701:2010 Nanotechnologies – Endotoxin test on nanomaterial samples for in vitro systems – Limulus amebocyte lysate (LAL) test
- 'ISO 4892-2'
  Plastics – Methods of exposure to laboratory light sources – Part 2: Xenon-arc lamps
- 'ISO/TS 80004-1:2015'
  ISO/TS 80004-1:2015 Nanotechnologies – Vocabulary – Part 1: Core terms
- 'ISO/TS 80004-2:2015'
  ISO/TS 80004-2:2015 Nanotechnologies – Vocabulary – Part 2: Nano-objects
- 'ISO/TS 80004-3:2010'
  ISO/TS 80004-3:2010 Nanotechnologies – Vocabulary – Part 3: Carbon nano-objects
- 'ISO/TS 80004-4:2011'
  ISO/TS 80004-4:2011 Nanotechnologies – Vocabulary – Part 4: Nanostructured materials
- 'ISO/TS 80004-5:2011'
  ISO/TS 80004-5:2011 Nanotechnologies – Vocabulary – Part 5: Nano/bio interface
- 'ISO/TS 80004-6:2015'
  ISO/TS 80004-6:2013 Nanotechnologies – Vocabulary – Part 6: Nano-object characterization
- 'ISO/TS 80004-7:2011'
  ISO/TS 80004-7:2011 Nanotechnologies – Vocabulary – Part 7: Diagnostics and therapeutics for healthcare

- 'ISO/TS 80004-8:2013'
  ISO/TS 80004-8:2013 Nanotechnologies – Vocabulary – Part 8: Nanomanufacturing processes
- 'IEC/TS 80004-9:2017'
  IEC/TS 80004-9:2017 Nanotechnologies – Vocabulary – Part 9: Nano-enabled electrotechnical products and systems
- 'ISO/TS 80004-11:2017'
  ISO/TS 80004-11:2017 Nanotechnologies – Vocabulary – Part 11: Nanolayer, nanocoating, nanofilm, and related terms
- 'ISO/TS 80004-12:2016'
  ISO/TS 80004-12:2016 Nanotechnologies – Vocabulary – Part 12: Quantum phenomena in nanotechnology
- 'ISO/TS 80004-13:2017'
  ISO/TS 80004-13:2017 Nanotechnologies – Vocabulary – Part 13: Graphene and related two-dimensional (2D) materials

OECD

The Organisation for Economic Co-operation and Development (OECD)

- 'OECD 29'
  OECD Series on Testing and Assessment No. 29 (23-Jul-2001): Guidance document on transformation/dissolution of metals and metal compounds in aqueous media [9152]
- 'OECD 39'
  OECD Guidance Document 39: Acute Inhalation Toxicity Testing
- 'OECD 53'
  Guidance document on simulated freshwater lentic field tests (outdoor microcosms and mesocosms)
- 'OECD 102'
  Melting point / Melting Range [1184]
- 'OECD 103'
  Boiling Point [62172, 1185]
- 'OECD 104'
  Vapour Pressure Curve [1186]
- 'OECD 105'
  Water Solubility [1187]
- 'OECD 106'
  Adsorption - Desorption Using a Batch Equilibrium Method [1188]
- 'OECD 107'
  Partition Coefficient (n-octanol / water), Shake Flask Method [1189]
- 'OECD 109'
  Density of Liquids and Solids [1190]
- 'OECD 110-A'
  Particle Size Distribution (effective hydrodynamic radius) [60079]
- 'OECD 110-B'
  Fibre Length and Diameter Distributions [60080]
- 'OECD 111'
  Hydrolysis as a Function of pH [1192]
- 'OECD 112'
  OECD Guideline 112 (Dissociation Constants in Water) [1193]
- 'OECD 114'
  Viscosity of Liquids [1309]
- 'OECD 115'
  Surface Tension of Aqueous Solutions [1195]
- 'OECD 116'
  Fat Solubility of Solid and Liquid Substances [1196]
- 'OECD 117'
  Partition Coefficient (n-octanol / water), HPLC Method [1197]
- 'OECD 121'
  Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC) [1198]
- 'OECD 122'
  Determination of pH, Acidity and Alkalinity [60450]
- 'OECD 123'
  Partition Coefficient (1-Octanol / Water), Slow-Stirring Method
- 'OECD 201 old'
  Alga, Growth Inhibition Test [1199] (before 23 march 2006)
- 'OECD 201'
  Freshwater Alga and Cyanobacteria, Growth Inhibition Test [61952]
- 'OECD 202'
  Daphnia sp. Acute Immobilisation Test [1200]

- 'OECD 203'
  Fish, Acute Toxicity Test [1201]
- 'OECD 204'
  Fish, Prolonged Toxicity Test: 14-day Study [1202] (not valid for testing from 2 April 2014)
- 'OECD 205'
  Avian Dietary Toxicity Test [1203]
- 'OECD 206'
  Avian Reproduction Test [1204]
- 'OECD 207'
  Earthworm, Acute Toxicity Tests [1205]
- 'OECD 208 old'
  Terrestrial Plants Test: Seedling Emergence and Seedling Growth Test [1206]
- 'OECD 208'
  Terrestrial Plants, Growth Test [61943]
- 'OECD 209'
  Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation) [61996]
- 'OECD 210'
  Fish, Early-Life Stage Toxicity Test [1208]
- 'OECD 211'
  aphnia magna Reproduction Test [1209]
- 'OECD 212'
  Fish, Short-term Toxicity Test on Embryo and Sac-Fry Stages [1210]
- 'OECD 213'
  Honeybees, Acute Oral Toxicity Test [1211]
- 'OECD 214'
  Honeybees, Acute Contact Toxicity Test [1212]
- 'OECD 215'
  Fish, Juvenile Growth Test [1213]
- 'OECD 216'
  Soil Microorganisms: Nitrogen Transformation Test [1214]
- 'OECD 217'
  Soil Microorganisms: Carbon Transformation Test [1215]
- 'OECD 218'
  Sediment-Water Chironomid Toxicity Test Using Spiked Sediment [1216]
- 'OECD 219'
  Sediment-Water Chironomid Toxicity Test Using Spiked Water [1217]
- 'OECD 220'
  Enchytraeid Reproduction Test [1218]
- 'OECD 221'
  Lemna sp. Growth Inhibition Test [1219]
- 'OECD 222'
  Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei) [1220]
- 'OECD 223'
  Avian Acute Oral Toxicity Test [1221]
- 'OECD 224'
  Determination of the Inhibition of the Activity of Anaerobic Bacteria – Reduction of Gas Production from Anaerobically Digesting (Sewage) Sludge [8305]
- 'OECD 225'
  Sediment-Water Lumbriculus Toxicity Test Using Spiked Sediment [61053]
- 'OECD 226'
  Predatory Mite (Hypoaspis (Geolaelaps) Aculeifer) Reproduction Test in Soil [61944]
- 'OECD 227'
  Terrestrial Plant Test: Vegetative Vigour Test [1308]
- 'OECD 228'
  Determination of Developmental Toxicity of a Test Chemical to Dipteran Dung Flies (Scathophaga stercoraria L. (Scathophagidae) and Musca autumnalis De Geer (Muscidae)) [61945]
- 'OECD 229'
  Fish Short Term Reproduction Assay [62057]
- 'OECD 230'
  21-day Fish Assay: A Short Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition [62058]
- 'OECD 231'
  The Amphibian Metamorphosis Assay [62059]
- 'OECD 232'
  Collembolan Reproduction Test in Soil [61946]
- 'OECD 233'
  Sediment-Water Chironomid Life-Cycle Toxicity Test Using Spiked Water or Spiked Sediment [61056]

- 'OECD 234'
  Fish Sexual Development Test [62060]
- 'OECD 235'
  Chironomus sp., Acute Immobilisation Test [61975]
- 'OECD 236'
  Fish embryo acute toxicity (FET) test [60883]
- 'OECD 237 '
  Honey bee (Apis mellifera) Larval Toxicity Test, Single Exposure [61947]
- 'OECD 238'
  Sediment-free Myriophyllum spicatum Toxicity Test [61950]
- 'OECD 239'
  Water-Sediment Myriophyllum spicatum Toxicity Test [61951]
- 'OECD 240'
  Medaka Extended One Generation Reproduction Test (MEOGRT) [62061]
- 'OECD 241'
  The Larval Amphibian Growth and Development Assay (LAGDA) [62062]
- 'OECD 242'
  Potamopyrgus antipodarum Reproduction Test [64806]
- 'OECD 243'
  Lymnaea stagnalis Reproduction Test [64807]
- 'OECD 245'
  Honey Bee (Apis mellifera L.), Chronic Oral Toxicity Test (10-Day Feeding) [64823]
- 'OECD 246'
  Bumblebee, Acute Contact Toxicity Test [64824]
- 'OECD 247'
  Bumblebee, Acute Oral Toxicity Test [64825]
- 'OECD 301-A'
  Ready Biodegradability: DOC Die Away Test [1222]
- 'OECD 301-B'
  Ready Biodegradability: CO2 Evolution Test [1224]
- 'OECD 301-C'
  Ready Biodegradability: Modified MITI Test (I) [1225]
- 'OECD 301-D'
  Ready Biodegradability: Closed Bottle Test [1226]
- 'OECD 301-E'
  Ready biodegradability: Modified OECD Screening Test [1227]
- 'OECD 301-F'
  Ready Biodegradability: Manometric Respirometry Test [1228]
- 'OECD 302-A'
  Inherent Biodegradability: Modified SCAS Test [1229]
- 'OECD 302-B'
  Inherent biodegradability: Zahn-Wellens/EMPA Test [1230]
- 'OECD 302-C'
  Inherent Biodegradability: Modified MITI Test (II) [1231]
- 'OECD 302-D'
  Draft (Inherent Biodegradability - Concawe Test) [1232]
- 'OECD 303-A'
  Simulation Test - Aerobic Sewage Treatment. A: Activated Sludge Units [1233]
- 'OECD 303-B'
  Simulation Test - Aerobic Sewage Treatment. B. Biofilms [1234]
- 'OECD 304-A'
  Inherent Biodegradability in Soil [1235]
- 'OECD 305'
  OECD Guideline 305 (Bioconcentration: Flow-through Fish Test) [1236]
- 'OECD 305-I'
  Bioaccumulation in Fish: Aqueous and Dietary Exposure -I: Aqueous Exposure Bioconcentration Fish Test [60713]
- 'OECD 305-II'
  Bioaccumulation in Fish: Aqueous and Dietary Exposure -II: Minimised Aqueous Exposure Fish Test [60714]
- 'OECD 305-III'
  Bioaccumulation in Fish: Aqueous and Dietary Exposure -III: Dietary Exposure Bioaccumulation Fish Test [60715]
- 'OECD 305-A'
  Bioaccumulation: Sequential Static Fish Test [1237]
- 'OECD 305-B'
  Bioaccumulation: Semi-static Fish Test [1238]

- 'OECD 305-C'
  Bioaccumulation: Test for the Degree of Bioconcentration in Fish [1239]
- 'OECD 305-D'
  Bioaccumulation: Static Fish Test [1240]
- 'OECD 305-E'
  Bioaccumulation: Flow-through Fish Test [1241]
- 'OECD 306'
  Biodegradability in Seawater[1242]
- 'OECD 307'
  Aerobic and Anaerobic Transformation in Soil [1243]
- 'OECD 308'
  Aerobic and Anaerobic Transformation in Aquatic Sediment Systems [1244]
- 'OECD 309'
  Aerobic Mineralisation in Surface Water - Simulation Biodegradation Test [1245]
- 'OECD 310'
  Ready Biodegradability - CO2 in Sealed Vessels (Headspace Test) [1246]
- 'OECD 311'
  Anaerobic Biodegradability of Organic Compounds in Digested Sludge: Measurement of Gas Production [1247]
- 'OECD 312'
  Leaching in Soil Columns [1248]
- 'OECD 314-A'
  Simulation Tests to Assess the Biodegradability of Chemicals in Wastewater. A: Biodegradation in a Sewer System [61241]
- 'OECD 314-B'
  Simulation Tests to Assess the Biodegradability of Chemicals in Wastewater. B: Biodegradation in Activated Sludge [61242]
- 'OECD 314-C'
  Simulation Tests to Assess the Biodegradability of Chemicals in Wastewater. C: Mineralization and Transformation in Anaerobic Digester Sludge [61243]
- 'OECD 314-D'
  Simulation Tests to Assess the Biodegradability of Chemicals in Wastewater. D: Biodegradation in Treated Effluent-Surface Water Mixing Zone [61244]
- 'OECD 314-E'
  Simulation Tests to Assess the Biodegradability of Chemicals in Wastewater. E: Biodegradation in Untreated Wastewater-Surface Water Mixing Zone [61245]
- 'OECD 315'
  Bioaccumulation in Sediment-dwelling Benthic Oligochaetes [60723]
- 'OECD 316'
  Phototransformation of Chemicals in Water - Direct Photolysis [61997]
- 'OECD 317'
  Bioaccumulation in Terrestrial Oligochaetes [60801]
- 'OECD 318'
  Dispersion stability of nanomaterial in simulated environmental media
- 'OECD 412'
  Subacute Inhalation Toxicity: 28-Day Study.
- 'OECD 413'
  Subchronic Inhalation Toxicity: 90-Day study
- 'OECD 417'
  Toxicokinetics[1265]
- 'OECD No. 29'
  OECD Series on Testing and Assessment No. 29 (23-Jul-2001): Guidance document on transformation/dissolution of metals and metal compounds in aqueous media [9152]
- 'OECD 427'
  Skin Absorption: In Vivo Method [1275]
- 'OECD 428'
  Skin Absorption: In Vitro Method [1276]
- 'OECD 401'
  Acute Oral Toxicity [1249]
- 'OECD 408'
  TG 408 is an OECD validated method providing information on health hazard likely to arise from exposure to test substance via oral administration.
- 'OECD 420'
  Acute Oral Toxicity - Fixed Dose Method [1268]
- 'OECD 423'
  Acute Oral toxicity - Acute Toxic Class Method [1271]
- 'OECD 425'
  OECD Guideline 425 (Acute Oral Toxicity: Up-and-Down Procedure) [1273]
- 'OECD WNT 3.11'
  Project 3.11: New TG for nanomaterial removal from wastewater
- 'OECD 476'
  In Vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes

- 'OECD 487'
  In Vitro Mammalian Cell Micronucleus Test
- 'OECD 488'
  Transgenic rodent (TGR) somatic and germ cell gene mutation assays
- 'OECD 489'
  OECD Test Guideline 489: In vivo alkaline single-cell gel electrophoresis assay for DNA strand breaks (Comet assay)
- 'OECD 490'
  OECD 490, In Vitro Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene,
- 'OECD 473'
  In Vitro Mammalian Chromosomal Aberration Test

ASTM

American Society for Testing and Materials. https://www.astm.org

- 'ANSI/ASTM E 70-700'
  ANSI/ASTM E 70-7700 ?? [9003]
- 'ASTM D88'
  Standard Test Method for Saybolt Viscosity [60143]
- 'ASTM D445'
  Standard Test Method for Kinematic Viscosity of Transparent and Opaque Liquids (and Calculation of Dynamic Viscosity) [60144]
- 'ASTM D562'
  Standard Test Method for Consistency of Paints Measuring Krebs Unit (KU) Viscosity Using a Stormer-Type Viscometer [60145]
- 'ASTM D1200'
  Standard Test Method for Viscosity by Ford Viscosity Cup [60146]
- 'ASTM D1293'
  Standard Test Methods for pH of Water [9002]
- 'ASTM D2196'
  Standard Test Methods for Rheological Properties of Non-Newtonian Materials by Rotational (Brookfield type) Viscometer [60147]
- 'ASTM D2983'
  Standard Test Method for Low-Temperature Viscosity of Lubricants Measured by Brookfield Viscometer [60148]
- 'ASTM D4486'
  Standard Test Method for Kinematic Viscosity of Volatile and Reactive Liquids [60149]
- 'ASTM D1895'
  Standard Test Methods for Apparent Density, Bulk Factor, and Pourability of Plastic Materials [58575]
- 'ASTM E1688'
  Standard guide for determination of bioaccumulation of sediment-associated contaminants by benthic invertebrates [2160]
- 'ASTM E1367 old1 '
  10-day Static Sediment Toxicity Test (Media: Sediment-marine) [37]
- 'ASTM E1367 old2'
  10-day Static Sediment Toxicity Test (Media: Sediment-estuarine) [36]
- 'ASTM E1367-03'
  Standard Test Method for Measuring the Toxicity of Sediment-Associated Contaminants with Estuarine and Marine Invertebrates [61883]
- 'ASTM E1383'
  Sediment Toxicity Test (Media: Sediment-freshwater) [38]
- 'ASTM E1525'
  Sediment Toxicity Test [39]
- 'ASTM E1611 old1'
  Sediment Toxicity Test (Media: Sediment-marine) [41]
- 'ASTM E1611 old2'
  Sediment Toxicity Test (Media: Sediment-estuarine) [40]
- 'ASTM E1611'
  Standard Guide for Conducting Sediment Toxicity Tests with Polychaetous Annelids [61882]
- 'ASTM E1688 old1'
  Sediment Toxicity Test (Media: Sediment-freshwater) [43]
- 'ASTM E1688 old2'
  Sediment Toxicity Test (Media: Sediment-marine) [42]
- 'ASTM E1688-10'
  Standard Guide for Determination of the Bioaccumulation of Sediment-Associated Contaminants by Benthic Invertebrates [??]
- 'ASTM E1706 old1'
  Sediment Toxicity Test (Media: Sediment-freshwater) [44]
- 'ASTM E1706 old2'
  Test Method for Measuring the Toxicity of Sediment-Associated Contaminants with Freshwater Invertebrates [35]

- 'ASTM E1706-05'
  Standard Test Method for Measuring the Toxicity of Sediment-Associated Contaminants with Freshwater Invertebrates [61884]
- 'ASTM E1676 old1'
  Standard Guide for Conducting Laboratory Soil Toxicity or Bioaccumulation Tests with the Lumbricid Earthworm Eisenia fetida [6600]
- 'ASTM E1676-12'
  Standard Guide for Conducting Laboratory Soil Toxicity or Bioaccumulation Tests with the Lumbricid Earthworm Eisenia Fetida and the Enchytraeid Potworm Enchytraeus albidus [61887]

EPA

Environmental Protection Agency

- 'OPPTS 830.6302'
  Color[4762]
- 'OPPTS 830.6303'
  Physical State [4763]
- 'OPPTS 830.6304'
  Odor[4764]
- 'OPPTS 830.7000'
  pH[4100]
- 'OPPTS 830.7100'
  Viscosity[3890]
- 'OPPTS 830.7200'
  Melting Point / Melting Range [4083]
- 'OPPTS 830.7220'
  Boiling Point / Boiling Range [4084]
- 'OPPTS 830.7300'
  Density / Relative Density / Bulk Density [4085]
- 'OPPTS 830.7370'
  Dissociation constants in water [3889]
- 'OPPTS 830.7520'
  Particle Size, Fiber Length, and Diameter Distribution [4088]
- 'OPPTS 830.7550'
  Partition Coefficient, n-octanol / H2O, Shake Flask Method [430]
- 'OPPTS 830.7560'
  Partition Coefficient, n-octanol / H2O, Generator Column Method [432]
- 'OPPTS 830.7570'
  Partition Coefficient, n-octanol / H2O, Estimation by Liquid Chromatography [433]
- 'OPPTS 830.7840'
  Water Solubility [434]
- 'OPPTS 830.7950'
  Vapor Pressure [1315]
- 'OPPTS 830.7860'
  Water Solubility Generator Column Method [435]
- 'OPPTS 835.1110'
  Activated Sludge Sorption Isotherm [436]
- 'OPPTS 835.1210'
  Soil Thin Layer Chromatography [437]
- 'OPPTS 835.1220'
  Sediment and Soil Adsorption / Desorption Isotherm [438]
- 'OPPTS 835.2110'
  Hydrolysis as a Function of pH [4065]
- 'OPPTS 835.2120'
  Hydrolysis of Parent and Degradates as a Function of pH at 25°C [4066]
- 'OPPTS 835.2130'
  Hydrolysis as a Function of pH and Temperature [4067]
- 'OPPTS 835.2210'
  Direct Photolysis Rate in Water by Sunlight [439]
- 'OPPTS 835.2310'
  Maximum Direct Photolysis Rate in Air from UV/Visible Spectroscopy [440]
- 'OPPTS 835.3100'
  Aerobic Aquatic Biodegradation [441]
- 'OPPTS 835.3110'
  Ready Biodegradability [442]

- 'OPPTS 835.3120'
  Sealed Vessel Carbon Dioxide Production Test [443]
- 'OPPTS 835.3140'
  Ready Biodegradability – CO2 in Sealed Vessels (Headspace Test) [60758]
- 'OPPTS 835.3160'
  Biodegradability in Sea Water [61248]
- 'OPPTS 835.3170'
  Shake Flask Die-away Test [444]
- 'OPPTS 835.3180'
  Sediment / Water Microcosm Biodegradation Test [445]
- 'OPPTS 835.3190'
  Aerobic Mineralisation in Surface Water - Simulation Biodegradation Test [61249]
- 'OPPTS 835.3200'
  Zahn-Wellens / EMPA Test [446]
- 'OPPTS 835.3210 '
  Inherent Biodegradability: Modified SCAS Test [447]
- 'OPPTS 835.3215'
  Inherent Biodegradability - Concawe Test [60757]
- 'OPPTS 835.3220'
  Porous Pot Test [448]
- 'OPPTS 835.3240'
  Simulation Test - Aerobic Sewage Treatment: A. Activated Sludge Units [61250]
- 'OPPTS 835.3260'
  Simulation Test - Aerobic Sewage Treatment: B. Biofilms [61251]
- 'OPPTS 835.3300'
  Soil Biodegradation [449]
- 'OPPTS 835.4300'
  Aerobic Aquatic Metabolism [4069]
- 'OPPTS 835.3400'
  Anaerobic Biodegradability of Organic Chemicals [450]
- 'OPPTS 835.3420'
  Anaerobic Biodegradability of Organic Compounds in Digested Sludge: By Measurement of Gas Production [60759]
- 'OPPTS 835.4100'
  Aerobic Soil Metabolism [60724]
- 'OPPTS 835.4200'
  Anaerobic Soil Metabolism [60725]
- 'OPPTS 835.4400'
  Anaerobic Aquatic Metabolism [451]
- 'OPPTS 835.5045'
  Modified SCAS Test for Insoluble and Volatile Chemicals [452]
- 'OPPTS 835.5154 '
  Anaerobic Biodegradability in the Subsurface [453]
- 'OPPTS 835.5270'
  Indirect Photolysis Screening Test: Sunlight Photolysis in Waters Containing Dissolved Humic Substances [454]
- 'OPPTS 850.1010'
  Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids [455]
- 'OPPTS 850.1020'
  Gammarid Acute Toxicity Test [456]
- 'OPPTS 850.1025'
  Bivalve Acute Toxicity (shell deposition test) [457]
- 'OPPTS 850.1035'
  Mysid Acute Toxicity Test [458]
- 'OPPTS 850.1045'
  EPA OPPTS 850.1045 (Penaeid Acute Toxicity Test) [459]
- 'OPPTS 850.1055'
  Bivalve Acute Toxicity Test (embryo larval) [460]
- 'OPPTS 850.1075'
  Freshwater and Saltwater Fish Acute Toxicity Test [461]
- 'OPPTS 850.1085'
  Fish Acute Toxicity Test mitigated by humic acid [462]
- 'OPPTS 850.1300'
  Daphnid Chronic Toxicity Test [463]
- 'OPPTS 850.1350'
  Mysid Chronic Toxicity Test [464]

- 'OPPTS 850.1400'
  Fish Early-life Stage Toxicity Test [465]
- 'OPPTS 850.1500'
  Fish Life Cycle Toxicity [466]
- 'OPPTS 850.1710'
  Oyster Bioconcentration Test [467]
- 'OPPTS 850.1730'
  Fish Bioconcentration Test [468]
- 'OPPTS 850.1735'
  Whole Sediment Acute Toxicity of Invertebrates, freshwater [469]
- 'OPPTS 850.1740'
  Whole Sediment Acute Toxicity of Invertebrates, marine [470]
- 'OPPTS 850.1790'
  Chironomid Sediment Toxicity Test [471]
- 'OPPTS 850.1800'
  Tadpole/Sediment Subchronic Toxicity Test [472]
- 'OPPTS 850.1850'
  Aquatic Food Chain Transfer [473]
- 'OPPTS 850.2100'
  Avian Acute Oral Toxicity Test [474]
- 'OPPTS 850.2200'
  Avian Dietary Toxicity Test [475]
- 'OPPTS 850.2300'
  Avian Reproduction Test [476]
- 'OPPTS 850.2400'
  Wild Mammal Acute Toxicity Test [477]
- 'OPPTS 850.2450'
  Terrestrial (soil core) Microcosm Test [478]
- 'OPPTS 850.2500'
  Field Testing for Terrestrial Wildlife [479]
- 'OPPTS 850.3020'
  Honey Bee Acute Contact Toxicity [480]
- 'OPPTS 850.3030'
  Honey Bee Toxicity of Residues on Foliage [481]
- 'OPPTS 850.3040'
  Field Testing for Pollinators [482]
- 'OPPTS 850.4000'
  Background - Nontarget Plant Testing [483]
- 'OPPTS 850.4025'
  Target Area Phytotoxicity [484]
- 'OPPTS 850.4100'
  Terrestrial Plant Toxicity Tier I (seedling emergence) [485]
- 'OPPTS 850.4150'
  Terrestrial Plant Toxicity Tier I (vegetative vigor) [486]
- 'OPPTS 850.4200'
  Seed Germination/Root Elongation Toxicity Test [487]
- 'OPPTS 850.4225'
  Seedling Emergence Tier II [488]
- 'OPPTS 850.4230'
  Early Seedling Growth Toxicity Test [489]
- 'OPPTS 850.4250'
  Vegetative Vigor Tier II [490]
- 'OPPTS 850.4300'
  Terrestrial Plants Field Study Tier III [491]
- 'OPPTS 850.4400'
  Aquatic Plant Toxicity Test using Lemna spp. Tiers I & II [492]
- 'OPPTS 850.4450'
  Aquatic Plants Field Study (Tier III) [493]
- 'OPPTS 850.4600'
  Rhizobium - Legume Toxicity [494]
- 'OPPTS 850.4800'
  Plant Uptake & Translocation Test [495]
- 'OPPTS 850.5100'
  Soil Microbial Community Toxicity Test [496]

- 'OPPTS 850.5400'
  Algal Toxicity, Tiers I and II [497]
- 'OPPTS 850.6200'
  Earthworm Subchronic Toxicity Test [498]
- 'OPPTS 850.6800'
  Modified Activated Sludge, Respiration Inhibition Test for Sparingly Soluble Chemicals [499]
- 'OPPTS 870.7485'
  Metabolism and Pharmacokinetics[542]
- 'OPPTS 870.8223'
  Pharmacokinetic Test [4469]
- 'OPPTS 870.8320'
  Oral/dermal pharmacokinetics [4470]
- 'OTS 795.45'
  Inherent Biodegradability: Modified SCAS Test for Chemical Substances that are Water Insoluble or Water Insoluble and Volatile [555]
- 'OTS 795.54'
  Anaerobic Biodegradability in the Subsurface [556]
- 'OTS 795.70'
  Indirect Photolysis Screening Test: Sunlight Photolysis in Waters Containing Dissolved Humic Substances [557]
- 'OTS 795.150'
  Earthworm Subchronic Toxicity Test [550]
- 'OTS 795.1200'
  Gammarid Acute Toxicity Test [548]
- 'OTS 795.1350'
  Chironomid Sediment Toxicity Test [549]
- 'OTS 795.1700'
  Modified Activated Sludge, Respiration Inhibition Test for Sparingly Soluble Chemicals [551]
- 'OTS 796.2700'
  Soil Thin Layer Chromatography [558]
- 'OTS 796.2750'
  Sediment and Soil Adsorption Isotherm [559]
- 'OTS 796.3100'
  Aerobic Aquatic Biodegradation [560]
- 'OTS 796.3140'
  Anaerobic Biodegradability of Organic Chemicals [561]
- 'OTS 796.3180'
  Ready Biodegradability: Modified AFNOR Test [562]
- 'OTS 796.3200'
  Ready Biodegradability: Closed Bottle Test [563]
- 'OTS 796.3220'
  Ready Biodegradability: Modified MITI Test(I) [564]
- 'OTS 796.3240'
  Ready Biodegradability: Modified OECD Screening Test [565]
- 'OTS 796.3260'
  Ready Biodegradability: Modified Sturm Test [566]
- 'OTS 796.3340'
  Inherent Biodegradability: Modified SCAS Test [567]
- 'OTS 796.3360'
  Inherent Biodegradability: Modified Zahn-Wellens Test [568]
- 'OTS 796.3400'
  Soil Biodegradation [569]
- 'OTS 796.3500'
  Hydrolysis as a Function of pH at 25°C [570]
- 'OTS 796.3510'
  Hydrolysis as a Function of pH and Temperature [571]
- 'OTS 796.3700'
  Direct Photolysis Rate in Water by Sunlight [572]
- 'OTS 796.3800'
  Maximum Direct Photolysis Rate in Air from UV/Visible Spectroscopy [573]
- 'OTS 797.1000'
  Fish Early-life Stage Toxicity Test [574]
- 'OTS 797.1050'
  Algal Toxicity, Tiers I and II [575]
- 'OTS 797.1160'
  Aquatic Plant Toxicity Test using Lemna spp. Tiers I & II [576]

- 'OTS 797.1300'
  Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids [577]
- 'OTS 797.1330'
  Daphnid Chronic Toxicity Test [578]
- 'OTS 797.1400'
  Fish Acute Toxicity Test [579]
- 'OTS 797.1460'
  Fish Acute Toxicity Test mitigated by humic acid [580]
- 'OTS 797.1520'
  Fish Bioconcentration Test-Rainbow Trout [581]
- 'OTS 797.1800'
  Oyster Acute Toxicity test (shell deposition) [582]
- 'OTS 797.1830'
  Oyster Bioconcentration Test [583]
- 'OTS 797.1930'
  Mysid Acute Toxicity Test [584]
- 'OTS 797.1950'
  Mysid Chronic Toxicity Test [585]
- 'OTS 797.1970'
  Penaeid Acute Toxicity Test [586]
- 'OTS 797.1995'
  Tadpole/Sediment Subchronic Toxicity Test [587]
- 'OTS 797.2050'
  Avian Dietary Toxicity Test [588]
- 'OTS 797.2130'
  Avian Reproduction Test [589]
- 'OTS 797.2150'
  Avian Reproduction Test [590]
- 'OTS 797.2175'
  Avian Acute Oral Toxicity Test [591]
- 'OTS 797.2750'
  Seed Germination/Root Elongation Toxicity Test [592]
- 'OTS 797.2800'
  Early Seedling Growth Toxicity Test [593]
- 'OTS 797.2850'
  Plant Uptake & Translocation Test [594]
- 'OTS 797.2900'
  Rhizobium - Legume Toxicity [595]
- 'OTS 797.3700'
  Soil Microbial Community Toxicity Test [596]
- 'OTS 797.3775'
  Terrestrial (soil core) Microcosm Test [597]
- 'OTS 798.7485'
  Metabolism and Pharmacokinetics[636]
- 'GSD N 161-1'
  Hydrolysis[4064]
- 'GSD N 161-2'
  Photodegradation Studies in Water [375]
- 'GSD N 161-3'
  Photodegradation Studies on Soil [376]
- 'GSD N 161-4'
  Photodegradation Studies in Air [377]
- 'GSD N 162-3'
  Pesticide Guideline (Anaerobic Aquatic Metabolism) [637]
- 'GSD N 162-4'
  Pesticide Guideline (Aerobic Aquatic Metabolism) [638]
- 'OPP 71-1'
  Avian Acute Oral Toxicity Test [394]
- 'OPP 71-2'
  Avian Dietary Toxicity Test [395]
- 'OPP 71-3'
  Wild Mammal Acute Toxicity Test [396]
- 'OPP 71-4 '
  Avian Reproduction Test [397]

- 'OPP 71-5'
  Field Testing for Terrestrial Wildlife [398]
- 'OPP 72-1'
  Fish Acute Toxicity Test [399]
- 'OPP 72-2'
  Aquatic Invertebrate Acute Toxicity Test [400]
- 'OPP 72-3'
  Estuarine/Marine Fish, Mollusk, or Shrimp Acute Toxicity Test [401]
- 'OPP 72-4'
  Fish Early Life-Stage and Aquatic Invertebrate Life-Cycle Studies [402]
- 'OPP 72-5'
  Fish Life Cycle Toxicity [403]
- 'OPP 72-6'
  Aquatic Organism Accumulation Tests [404]
- 'OPP 81-1'
  Acute Oral Toxicity [405]
- 'OPP 85-1'
  Metabolism and Pharmacokinetics[426]
- 'OPP 85-3'
  Dermal Penetration [427]
- 'OPP 120-1'
  Background - Nontarget Plant Testing [378]
- 'OPP 121-1'
  Target Area Phytotoxicity [379]
- 'OPP 122-1 A'
  Terrestrial Plant Toxicity Tier I (seedling emergence) [381]
- 'OPP 122-1 B'
  Terrestrial Plant Toxicity Tier I (vegetative vigor) [382]
- 'OPP 122-1 C'
  Seed Germination/Root Elongation Toxicity Test [380]
- 'OPP 122-2'
  Algal Toxicity, Tiers I and II [383]
- 'OPP 123-1 A'
  Seedling Emergence Tier II [385]
- 'OPP 123-1 B'
  Early Seedling Growth Toxicity Test [384]
- 'OPP 123-1 C'
  Vegetative Vigor Tier II [386]
- 'OPP 123-3'
  Algal Toxicity, Tiers I and II [387]
- 'OPP 124-1'
  Terrestrial Plants Field Study Tier III [388]
- 'OPP 124-2'
  Aquatic Plants Field Study, Tier III [389]
- 'OPP 141-1'
  Honey Bee Acute Contact Toxicity [390]
- 'OPP 141-2'
  Honey Bee Toxicity of Residues on Foliage [391]
- 'OPP 141-5'
  Field Testing for Pollinators [392]
- 'OPP 165-4'
  Laboratory Studies of Pesticide Accumulation in Fish [393]
- 'EPA 600/R-94/024'
  Methods for measuring the toxicity and bioaccumulation of sediment-associated contaminants with freshwater invertebrates [2161]
- 'OPPTS 870.8340'
  Oral and Inhalation Pharmacokinetic Test [4471]
- 'OPPTS 870.8360'
  Pharmacokinetics of Isopropanol [4472]
- 'OPPTS 870.8380'
  Inhalation and Dermal Pharmacokinetics of Commercial Hexane [4473]
- 'OPPTS 870.8500'
  Toxicokinetic Test [4474]
- 'OTS 795.2230'
  Pharmacokinetic Test [4475]

- 'OTS 795.2280'
  Oral/Dermal Pharmacokinetics [4476]
- 'OTS 795.2300'
  Pharmacokinetic Test [4477]
- 'OTS 795.2310'
  Pharmacokinetics of Isopropanol [4478]
- 'OTS 795.2320'
  Inhalation and Dermal Pharmacokinetics of Commercial Hexane [4479]
- 'OTS 795.2350'
  Toxicokinetic Test [4480]
- 'OPPTS 870.7600'
  Dermal Penetration [543]
- 'OPPTS 870.8245'
  Dermal Pharmacokinetics of DGBE and DGBA [4481]
- 'OPPTS 870.8300'
  Dermal Absorption for Compounds that are Volatile and Metabolised to Carbon Monoxide [4482]
- 'OTS 795.2250'
  Dermal Pharmacokinetics of DGBE and DGBA [4483]
- 'OTS 795.2260'
  Dermal Absorption for Compounds that are Volatile and Metabolised to Carbon Monoxide [4484]
- 'OPPTS 870.1100'
  Acute Oral Toxicity [501]
- 'OTS 798.1175'
  Acute Oral Toxicity [600]
- 'SW-846.1311'
  SW-846 Test Method 1311: Toxicity Characteristic Leaching Procedure

DIN

German Institute for Standardization

- 'DIN 19733'
  [313]
- 'DIN 55992-1'
  Determination of a parameter for the dust formation of pigments and extenders - Part 1: Rotation method [9151]
- 'DIN 51366'
  Testing of mineral oil hydrocarbons - Measurement of kinematic viscosity by means of the Cannon-Fenske viscometer for opaque liquids [60153]
- 'DIN 51377'
  Testing of lubricants - Determination of the apparent viscosity of motor oils at low temperature from -5 °C to -35 °C - Using the cold-cranking simulator [60154]
- 'DIN 51562'
  Part 1 (Viscometry - Measurement of kinematic viscosity by means of the Ubbelohde viscometer - Part 1: Viscometer specification and measurement procedure) [60155]
- 'DIN 52007-2'
  Bitumen and bituminous binders - Determination of viscosity - Part 2: Measurement by drawn-sphere viscometer [60156]
- 'DIN 53015'
  Viscometry - Measurement of viscosity by means of the rolling ball viscometer by Höppler [60157]
- 'DIN 53019'
  Part 1 (Viscometry - Measurement of viscosities and flow curves by means of rotational viscometers - Part 1: Principles and measuring geometry) [60158]
- 'DIN 53177'
  Binders for paints and varnishes - Measurement of the dynamic viscosity of liquid resins; Resin solutions and oils by the capillary viscosimeter of isocelses type according to Ubbelohde [60159]
- 'DIN 53214'
  Testing of paints and varnishes - Determination of rheograms and viscosities by rotational viscometers [60160]
- 'DIN 33897-2'
  Workplace atmospheres - Determination of the dustiness of bulk materials - Part 2: Continuous Drop [5803]
- 'DIN 38412-27'
  Pseudomonas putida Zellvermehrungshemmtest [60849]
- 'DIN 38412-8'
  Pseudomonas Zellvermehrungshemmtest [315]
- 'DIN 38414'
  German standard methods for the examination of water, waste water and sludge – Sludge and sediments (group S) – Determination of the organically bound halogens amenable to extraction (S 17) [60850]

EU

- 'METHOD A.1'
  Melting / Freezing Temperature [646]

- 'METHOD A.2'
  Boiling Temperature [655]
- 'METHOD A.3'
  Relative Density [657]
- 'METHOD A.4'
  Vapour Pressure [658]
- 'METHOD A.5'
  Surface Tension [659]
- 'METHOD A.6'
  Water Solubility [660]
- 'METHOD A.8-1'
  Partition Coefficient - Shake Flask Method [60249]
- 'METHOD A.8-2'
  Partition Coefficient - HPLC Method [60250]
- 'METHOD A.23'
  Partition Coefficient (1-Octanol/Water): Slow-Stirring Method [60251]
- 'METHOD C.1'
  Acute Toxicity for Fish [706]
- 'METHOD C.2'
  Acute Toxicity for Daphnia [716]
- 'METHOD C.3'
  Algal Inhibition test [722]
- 'METHOD C.4-A'
  Determination of the "Ready" Biodegradability - Dissolved Organic Carbon (DOC) Die-Away Test [723]
- 'METHOD C.4-B'
  Determination of the "Ready" Biodegradability - Modified OECD Screening Test [724]
- 'METHOD C.4-C'
  Determination of the "Ready" Biodegradability - Carbon Dioxide Evolution Test [725]
- 'METHOD C.4-D'
  Determination of the "Ready" Biodegradability - Manometric Respirometry Test [726]
- 'METHOD C.4-E'
  Determination of the "Ready" Biodegradability - Closed Bottle Test [727]
- 'METHOD C.4-F'
  Determination of the "Ready" Biodegradability - MITI Test [728]
- 'METHOD C.5'
  Degradation: Biochemical Oxygen Demand [729]
- 'METHOD C.6'
  Degradation: Chemical Oxygen Demand [730]
- 'METHOD C.7'
  Degradation: Abiotic Degradation: Hydrolysis as a Function of pH [4063]
- 'METHOD C.8'
  Toxicity for Earthworms: Artificial Soil Test [731]
- 'METHOD C.9'
  Biodegradation: Zahn-Wellens Test [732]
- 'METHOD C.10'
  Biodegradation: Activated Sludge Simulation Test [707]
- 'METHOD C.10-A'
  Simulation Test Aerobic Sewage Treatment: Activated Sludge Units [61246]
- 'METHOD C.10-B'
  Simulation Test Aerobic Sewage Treatment: Biofilms [61247]
- 'METHOD C.11'
  Biodegradation: Activated Sludge Respiration Inhibition Test [708]
- 'METHOD C.12'
  Biodegradation: Modified SCAS Test [709]
- 'METHOD C.13'
  Bioconcentration: Flow-through fish test [710]
- 'METHOD C.14'
  Fish Juvenile Growth Test [711]
- 'METHOD C.15'
  Fish, Short-term Toxicity Test on Embryo and Sac-fry Stages [712]
- 'METHOD C.16'
  Honeybees - Acute Oral Toxicity Test [713]
- 'METHOD C.17'
  Honeybees - Acute Contact Toxicity Test [714]

- 'METHOD C.18'
  Adsorption / Desorption Using a Batch Equilibrium Method [715]
- 'METHOD C.19'
  Estimation of the Adsorption Coefficient (KOC) on Soil and Sewage Sludge Using High Performance Liquid Chromatography (HPLC) [4068]
- 'METHOD C.20'
  Daphnia magna Reproduction Test [717]
- 'METHOD C.21'
  Soil Microorganisms: Nitrogen Transformation Test [718]
- 'METHOD C.22'
  Soil Microorganisms: Carbon Transformation Test [719]
- 'METHOD C.23'
  Aerobic and Anaerobic Transformation in Soil [720]
- 'METHOD C.24 '
  Aerobic and Anaerobic Transformation in Aquatic Sediment Systems [721]
- 'METHOD C.27'
  Sediment-Water Chironomid Toxicity Test Using Spiked Sediment [61055]
- 'METHOD C.28'
  Sediment-Water Chironomid Toxicity Test Using Spiked Water [61057]
- 'METHOD C.29'
  Ready Biodegradability - CO2 in Sealed Vessels (Headspace Test) [60756]
- 'METHOD C.30'
  Bioaccumulation in Terrestrial Oligochaetes [60802]
- 'METHOD B.36'
  Toxicokinetics[693]
- 'METHOD B.44'
  Skin Absorption: In Vivo Method [61282]
- 'METHOD B.45'
  EU Method B.45 (Skin Absorption: In Vitro Method)
- 'METHOD B.1'
  Acute Toxicity (Oral) [663]
- 'METHOD B.1 bis'
  Acute Oral Toxicity - Fixed Dose Procedure [664]
- 'METHOD B.1 tris'
  Acute Oral Toxicity - Acute Toxic Class Method [665]

CIPAC

Collaborative International Pesticides Analytical Council

- 'CIPAC MT 3 '
  Specific gravity, density and weight per millilitre [60151]
- 'CIPAC MT 75'
  Determination of pH Values [9004]
- 'CIPAC MT 186'
  Bulk density [60236]
- 'CIPAC MT 191'
  Acidity or alkalinity of formulations [61869]
- 'CIPAC MT 192'
  Viscosity of liquids by rotational viscometry [60152]

BS

British standard

- 'BS 188'
  Methods for determination of the viscosity of liquids [60150]

EN

European standard

- 'EN 15051'
  Workplace atmospheres - Measurement of the dustiness of bulk materials - Requirements and reference test methods [58302]

- 'EN 15051-2'
  Workplace exposure. Measurement of the dustiness of bulk materials - Rotating drum method [61894]
- 'EN 15051-3'
  Workplace exposure - Measurement of the dustiness of bulk materials - Continuous drop method [61895]

ETAD

- 'Fermentation Tube Method'
  ETAD Fermentation Tube Method [644]

UK_BB

UK Blue Book methods

- 'UKBB 106'
  Methods for assessing the treatability of chemicals and industrial waste waters and their toxicity to sewage treatment processes [60855]

BBA

- 'BBA Part VI, 1-1'
  BBA Part VI, 1-1 [117]

SOP

Standard Operating Procedures

MediumDescriptor

Descriptors for both simulated physiological and environmental media

- 'Relevant aquatic medium'
  This medium descriptor indicates that the aquatic medium used in the assay is the actual water of the relevant compartment/zone.
- 'Relevant soil medium'
  This medium descriptor indicates that the soil medium used in the assay is the actual soil of the relevant compartment/zone.
- 'Relevant sediment medium'
  This medium descriptor indicates that the sediment medium used in the assay is the actual sediment of the relevant compartment/zone.
- 'Simulated lung airway lining fluid'
  Simulated lung airway lining fluid [ISO-TR 19057-2017, 10.3.2]
- 'Simulated lung macrophage phagolysosomal fluid'
  Simulated lung macrophage phagolysosomal fluid [ISO-TR 19057-2017, 10.3.3]
- 'Simulated saliva fluid'
  Simulated saliva (SS) [ISO-TR 19057-2017, 10.3.4.2]
- 'Simulated gastric fluid'
  Simulated gastric fluid [ISO-TR 19057-2017, 10.3.4.3]
- 'Simulated intestinal fluid'
  Simulated intestinal fluid [ISO-TR 19057-2017, 10.3.4.4]
- 'Simulated saliva (5min) + gastric fluid'
  Combined time dynamic fluid 1) simulated saliva fluid (5mins) then similated gastric fluid is added
- 'Simulated saliva (5min) + gastric(2h) + intestinal fluid'
  Combined time dynamic fluid, first simulated saliva fluid (5mins) then similated gastric fluid is added (2h) and then intestinal fluid is added
- 'Simulated sweat'
  Simulated sweat (SSW) [ISO-TR 19057-2017, 10.3.5]
- 'Simulated natural fresh waters'
  Simulated natural fresh waters [ISO-TR 19057-2017, 10.4.2]
- 'Simulated sea water'
  Simulated sea water [ISO-TR 19057-2017, 10.4.3]
- 'Simulated estuarine waters'
  Simulated estuarine waters [ISO-TR 19057-2017, 10.4.4]
- 'Simulated waste water'
- 'Cell culture media'
  cell model specific media
- 'Cell culture medium, pH 7.4'
  Cell Culture medium (pH 7.4)

- 'Cell culture medium, RPMI supplemented with 1% pen/strep, 10% FBS, 1% L-glutamine'
  RPMI 1640, also known as RPMI medium, is a growth medium used in cell culture.
  pen/strep, Penicillin-Streptomycin for cell culture
  Fetal bovine serum (FBS) is used as a growth supplement for the in vitro cell culture of eukaryotic cells.
  L-glutamine is an amino acid supplement commonly added to mammalian cell culture media. L-glutamine serves as an auxiliary energy source, especially when cells are rapidly dividing and also can be used by cells as a source of nitrogen for the synthesis of proteins, nucleic acids, etc.
- 'Cell culture medium, EMEM'
  Eagle's Minimum Essential Medium
- 'Cell culture medium, DMEM'
  Gibco Dulbecco's Modified Eagle Medium (DMEM) is a widely used basal medium for supporting the growth of many different mammalian cells.
- '5 mM sodium bicarbonate buffer, pH 5'
  E-G-1, batch dissolution test
- '5 mM sodium bicarbonate buffer, pH 7'
- '5 mM sodium bicarbonate buffer, pH 9'
- 'OECD TG318 medium + NOM, pH 4'
  E-G-1 Continuous flow system
- 'OECD TG318 medium + NOM, pH 7'
  E-G-1 Continuous flow system
- 'OECD TG318 medium + NOM, pH 9'
  E-G-1 Continuous flow system
- 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)'
  E-G-1 screening dispersion test, extended dispersion test
- 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)'
  E-G-1 screening dispersion test, extended dispersion test
- 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)'
  E-G-1 screening dispersion test, extended dispersion test
- 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 4)'
  E-G-1 extended dispersion test
- 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 7)'
  E-G-1 extended dispersion test
- 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 9)'
  E-G-1 extended dispersion test
- 'OECD TG318 alternative media/test media + NOM (0, 1, 10 Ca(NO3)2, pH 4, 7, 9) + SPM'
- 'Gut saline medium'
  E-G-2 (Fish gut saline)
- 'OECD TG301 mineral medium'
- 'OECD 303 Organic medium, synthetic sewage'
  E-G-4
- 'OECD 303 Organic medium, domestic sewage sludge'
  E-G-4
- 'OECD 303 Organic medium, activated sludge'
  E-G-4
- 'Ultra pure water'
- 'Buffered pure water'
  E-G-4:
- 'Sterile filtered water'
  Appropriate sources include Nanopure Diamond UV and Millipore MilliQ-filtered water (Jensen et al., 2011).
- '40 mg/L Ca; 6 mg/L Mg; 16 mg/L SO4;0.1 mg/L PO4; + mg/L SRNOM; pH7.5'
  E-G-5 Provide name for this composition!
  Foregs
- 'M9 medium'
  E-WS-2c-e'
- 'ISO artificial sediment'
  E-WS-2c-e'
- 'ISO artificial sediment + M9 medium'
- 'OECD 219 sediment'
- 'Smart and Barko medium'
  E-WS-2c-e', sediment, (CaCl2 · 2 H2O 91.7mg/l, MgSO4·7 H2O 69 mg/l, NaHCO3 58.4 mg/l, KHCO3 15.4 mg/l, pH (air equilibrium) 7.9)
- 'OECD 219 sediment + Smart and Barko medium'
- 'OECD 203 water'
- 'OECD 225 sediment'
- 'OECD 203 water + OECD 225 sediment'
- 'OECD 218 conforming water'
- 'OECD 218 sediment'
- 'OECD 218 conforming water + sediment'
- 'OECD 233 conforming water'

- 'OECD 233 sediment'
- 'OECD 233 conforming water + sediment'
- 'Natural marine/estuarine sediment + water'
- 'Natural freshwater + sediment'
- '0.01 mM CaCl2'
  E-S-3 Screening batch retention test.
- 'SimpleBox4nano freshwater'
- 'In vivo dispersion media'
- 'NANOGENTOX dispersion media'
  NANOGENOTX dispersion media: NANOGENOTOX dispersion protocol (Jensen et al., 2011).
  A 2.56 mg/ml stock dispersion is prepared by prewetting powder in 0.5 vol% ethanol (96% purity) followed by dispersion in 0.05 wt% BSA-water during 16 minutes of probe sonication. For harmonization of dispersion energy and stabilities it is recommended to produce a 6-8 ml dispersion in the 20 ml tall glass scintillation vials. It takes 15.36 mg to produce a 6 ml 2.56 mg/ml stock dispersion.
- 'Human blood serum (HBS)'
- 'deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2'
- 'Aerolisation medium'
  Gaseous medium used to aerolise the sample in. (like air. etc..)

BM_CYTOKINES

Descriptors for different cytokine biomarkers measured (might be moved to separate knowledgebse together with cell type descriptors.)

- 'TNF-A'
  Tumour necrosis factor-α (TNF-α)
- 'IL-1B'
  IL-1β
- 'IL-6'
  IL-6
- 'IL-8'
- 'IL-10'
- 'IL-12'
- 'IL-15'
- 'IL-18'
  Interleukin-18 (IL18, also known as interferon-gamma inducing factor) is a protein which in humans is encoded by the IL18 gene.
- 'IFN-y'
  IFN-γ
- 'LDH'
  lactate dehydrogenase (LDH) enzyme
- 'GLU'
  ß-glucuronidase (not sure if this is a cytokine biomarker?)
- 'MIP-1A'
  MIP-1α
- 'MCP-1'

BM_HEAT_SHOCK_PROTEINS

Descriptors for different heat shock proteins.

- 'HSP70'

SpinTrapDescriptor

Descriptors of spintraps.

- 'DMPO'
  5,5-Dimethyl-1-pyrroline-N-oxide
- 'CPH'
  cyclic hydroxylamine spin probe 1-hydroxy-3-carboxy-pyrrolidine
- 'Tempone- H'
  1-hydroxyl-2,2,6,6-tetramethyl-4-oxo-piperidine

AssayType

- in_vitro

- in_vivo
  an in vivo experiment is one performed in a living organism
- in_silico
  an in silico experiment is one performed on computer or via computer simulation

7.2 Defined classes

Class Assay is kind of EP_Owner

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Attributes

name	type	domain	inference	comment
document_uuid_s	: String			*Uniquely identifies an assay within a eNanoMapper database*
medium_descriptor	:: MediumDescriptor			
cell_line_descriptor	:: any Enumerate			*The specific type of cell line used for this assay. (in case the assay is cell line specific)*
parameters_log	: XML nodes			

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	False	
title	: String	assay_descriptor→**If**(md | md→AsString, guideline→**If**(gl | gl→AsString, "GENERIC"))	
guideline	:: any Enumerate	**nil**	
assay_descriptor	:: AssayDescriptor	**nil**	
abbreviation	: String	""	
is_eNanoMapper_assay	: Boolean	ByUser(document_uuid_s) **and** (document_uuid_s→Trim ≠ "")	
minimum_tier	:: TierLevel	TL1	
actual_tier	:: TierLevel	DeriveActualTier()	*The actual tier is the highest derived tier level for which the assay results may be used for. E.g. if the highest tier level = 2, this means that the results may be used at TL 1 and TL 2, but NOT TL 3.* *The highest tier level may depend on the medium used, duration etc. It is always equal or higher to the minimum tier.*

Operators

```
function Assay.CategoryEndpointDomain(): Enumerations [specialization]
|  ResultEndpointDomain()→Collect(ep | ep→Enumeration)→Unique

function Assay.ValueEndpointDomain(): Enumerates [specialization]
|  ResultEndpointDomain()

function Assay::ResultEndpointDomain():: Enumerates
|  Enumerations{}

function Assay::MediumDescriptorDomain():: MediumDescriptors
|  MediumDescriptors{}

function Assay::CellDescriptorDomain():: Enumerates
|  Enumerates{}

function Assay.DeriveActualTier(): TierLevel
|  minimum_tier
```

Defined composites

Any instance of `Assay` is composed of
- at most one `assay_medium` of any kind of Medium

Class `PC_Assay` is kind of `Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Class `'Small Angle Neutron Scattering assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Small Angle Neutron Scattering'	
abbreviation	: String	"SANS"	

Class `'Neutron Diffraction assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Neutron Diffraction'	
abbreviation	: String	"ND"	*Not official.*

Class `'Small Angle X-ray Scattering assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Small Angle X-ray Scattering'	
abbreviation	: String	"SAXS"	

Operators

```
function 'Small Angle X-ray Scattering assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_GRANULOMETRY{EP_INTENSITY_WEIGHTED_SIZE}
```

Class `'Wide-Angle X-ray Scattering assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Wide-Angle X-ray Scattering'	
abbreviation	: String	"WAXS"	

Class 'Dynamic Light Scattering assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.
Not sure of mapping WP3 template
- size distribution: monomodal, bimodal, multimodal
- peak1 volume diameter in (nm)
- peak1 relative intensity (%)
- peak 2 volume diameter in (nm)
- peak 2 relative intensity (%)
- peak 3 volume diameter in (nm)
- peak 3 relative intensity (%)

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Dynamic Light Scattering'	
abbreviation	: String	"DLS"	

Operators

```
function 'Dynamic Light Scattering assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_GRANULOMETRY{EP_INTENSITY_WEIGHTED_SIZE, EP_Z_AVERAGE_DIAMETER, EP_RELATIVE_INTENSITY, EP_DISPERSITY, EP_DERIVED_COUNT_RATE, EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER}

function 'Dynamic Light Scattering assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Ultra pure water', 'Sterile filtered water', 'Simulated sweat'}
```

Class 'Nanoparticle Tracking Analysis assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Nanoparticle Tracking Analysis'	
abbreviation	: String	"NTA/PTA"	

Operators

```
function 'Nanoparticle Tracking Analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER, PC_GRANULOMETRY::EP_DISPERSITY, PC_GRANULOMETRY::EP_DnPx_D1}

function 'Nanoparticle Tracking Analysis assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Sterile filtered water', 'Simulated intestinal fluid', 'Simulated sweat'}
```

Class 'Small rotating Drum assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Small rotating Drum'	
abbreviation	: String	"SRD"	*not official*

Operators

```
function 'Small rotating Drum assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_DUSTINESS→Enumerates
```

Class 'Vortext Shaker assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Vortex Shaker'	
abbreviation	: String	"VS"	

Operators

```
function 'Vortext Shaker assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_DUSTINESS→Enumerates
```

Class 'Scanning Electron Microscopy assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Scanning Electron Microscopy'	
abbreviation	: String	"SEM"	

Operators

```
function 'Scanning Electron Microscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_PRIMARY_PARTICLE_DIAMETER, EP_PRIMARY_PARTICLE_LENGTH, EP_DnPx_D1, EP_DnPx_D3, EP_ASSEMBLY_STRUCTURE_AGG, PC_RIGIDITY::EP_STATIC_BENDING_PERSISTENCE_LENGTH, EP_CONTOUR_LENGTH, EP_FERET_DIAMETER_D3, EP_
   GEODESIC_LENGTH_D3, EP_DYNAMIC_SHAPE_FACTOR}

function 'Scanning Electron Microscopy assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Sterile filtered water', 'NANOGENTOX dispersion media', 'Cell culture media', 'Aerolisation medium'}
```

Class 'Transmission Electron Microscopy assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Transmission Electron Microscopy'	
abbreviation	: String	"TEM"	

Operators

```
function 'Transmission Electron Microscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
| Enumerates{EP_ASPECT_RATIO_D1_D3, EP_ASPECT_RATIO_D3_D1, EP_ASSEMBLY_STRUCTURE_AGG, EP_ZETA_POTENTIAL, EP_CIRCULARITY, EP_ROUNDNESS, EP_SOLIDITY, EP_FERET_DIAMETER_D1, EP_FERET_DIAMETER_D3, EP_EQUIVALENT_CIRCLE_
    DIAMETER, EP_GEOMETRIC_MEAN_DIAMETER, EP_DYNAMIC_SHAPE_FACTOR} + PC_GRANULOMETRY{EP_GEODESIC_LENGTH_D3, EP_CONSTITUENT_PARTICLE_SIZE, EP_PRIMARY_PARTICLE_DIAMETER, EP_PRIMARY_PARTICLE_LENGTH, EP_DnPx_D1, EP_DnPx_
    D3}
```

```
function 'Transmission Electron Microscopy assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
| MediumDescriptors{'Sterile filtered water', 'NANOGENTOX dispersion media', 'Cell culture media', 'Aerolisation medium', 'Simulated saliva fluid', 'Simulated gastric fluid', 'Simulated intestinal fluid', 'Simulated
|    saliva (5min) + gastric fluid', 'Simulated saliva (5min) + gastric(2h) + intestinal fluid', 'Simulated sweat'}
```

Class 'Scanning Transmission Electron Microscopy assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Scanning Transmission Electron Microscopy'	
abbreviation	: String	"STEM"	

Operators

```
function 'Scanning Transmission Electron Microscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
| PC_GRANULOMETRY{EP_DnPx_D1, EP_DnPx_D3, EP_FERET_DIAMETER_D3} + PC_ASPECT_RATIO_SHAPE{EP_ASSEMBLY_STRUCTURE_AGG}
```

```
function 'Scanning Transmission Electron Microscopy assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
| MediumDescriptors{'Sterile filtered water', 'NANOGENTOX dispersion media', 'Cell culture media', 'Aerolisation medium'}
```

Class 'Brunauer-Emmett-Teller assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Brunauer-Emmett-Teller method'	
abbreviation	: String	"BET"	*What about SBET*

Operators

```
function 'Brunauer-Emmett-Teller assay'.ResultEndpointDomain(): Enumerates [specialization]
| PC_SPECIFIC_SURFACE_AREA{EP_MASS_SPECIFIC_SURFACE_AREA, EP_SBET, EP_VOLUME_SPECIFIC_SURFACE_AREA, EP_MASS_MICROPOROSITY_SURFACE, EP_MASS_EXTERNAL_SURFACE} + PC_POROSITY{EP_PORE_RADIUS, EP_SPECIFIC_PORE_VOLUME}
```

Class 'Volumetric Centrifugation Method assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Volumetric Centrifugation Method'	
abbreviation	: String	"VCM"	

Operators

```
function 'Volumetric Centrifugation Method assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_DENSITY{EP_EFFECTIVE_DENSITY}
```

Class 'ElectroSpray-Differential Mobility Analysis assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'ElectroSpray-Differential Mobility Analysis'	
abbreviation	: String	"ES-DMA"	

Operators

```
function 'ElectroSpray-Differential Mobility Analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_GRANULOMETRY{EP_ELECTRICAL_MOBILITY_EQ_SPHERE_DIAMETER, EP_FULL_WIDTH_AT_HALF_MAXIMUM}
```

Class 'Sears titration assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Sears titration'	

Operators

```
function 'Sears titration assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_SPECIFIC_SURFACE_AREA{EP_MASS_SPECIFIC_SURFACE_AREA, EP_TITRATOR_VOLUME}
```

Class 'Drop shape analysis assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Drop shape analysis'	
abbreviation	: String	"DSA"	

Operators

```
function 'Drop shape analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_SURFACE_TENSION{EP_WATER_CONTACT_ANGLE}
```

```
function 'Drop shape analysis assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Sterile filtered water'}
```

Class 'X-ray Photoelectron Spectroscopy assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'X-ray Photoelectron Spectroscopy'	
abbreviation	: String	"XPS"	

Operators

```
function 'X-ray Photoelectron Spectroscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_COMPOSITION{EP_ELEMENTAL_COMPOSITION_ATOM_PERC}
```

Class 'Helium pycnometry assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Helium pycnometry'	

Operators

```
function 'Helium pycnometry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_DENSITY{EP_SKELETAL_DENSITY}
```

Class 'Analytical Ultracentrifugation assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.
Not sure of mapping WP3 template
- Peak-diameter of mass-weighted distribution (nm) ?
- Half height peak width (nm)
- Mass weighted mean diameter (nm)?

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Analytical Ultracentrifugation'	
abbreviation	: String	"AUC"	

Operators

```
function 'Analytical Ultracentrifugation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_GRANULOMETRY{EP_FULL_WIDTH_AT_HALF_MAXIMUM, EP_DmPx_D1, EP_DnPx_D1}
```

Class 'CHN analysis assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.
Purity tijdelijk toegevoegd ter controle..

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'CHN-Analysis'	
abbreviation	: String	"CHN"	

Operators

```
function 'CHN analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC}
```

Class 'Inductively Coupled Plasma Mass Spectrometry assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Inductively Coupled Plasma Mass Spectrometry'	
abbreviation	: String	"ICP-MS"	

Operators

```
function 'Inductively Coupled Plasma Mass Spectrometry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_COMPOSITION{EP_ELEMENTAL_COMPOSITION_MASS_CONC}
```

Class 'X-ray diffraction assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'X-ray diffraction'	
abbreviation	: String	"XRD"	

Operators

```
function 'X-ray diffraction assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_CRYSTALLINE_PHASE{EP_MINERAL_NAME, EP_SPACE_GROUP} + PC_GRANULOMETRY{EP_DnPx_D1, EP_DnPx_D3}

function 'X-ray diffraction assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Sterile filtered water', 'Simulated sweat'}
```

Class 'Batch Dissolution assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'ISO 19057:2017'	
assay_descriptor	: AssayDescriptor	'Static dissolution system'	

Operators

```
function 'Batch Dissolution assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_WATER_SOL{EP_DISSOLUTION_MASS_LOSS, EP_DISSOLUTION_HALF_TIME, EP_TRANSFORMATION_D1, EP_TRANSFORMATION_D3, EP_TRANSFORMATION_MORPHOLOGY}

function 'Batch Dissolution assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Simulated lung airway lining fluid', 'Simulated lung macrophage phagolysosomal fluid', 'Simulated saliva fluid', 'Simulated gastric fluid', 'Simulated intestinal fluid', 'Simulated saliva (5min) +
|     gastric fluid', 'Simulated saliva (5min) + gastric(2h) + intestinal fluid', 'Simulated sweat'} + MediumDescriptors{'5 mM sodium bicarbonate buffer, pH 5', '5 mM sodium bicarbonate buffer, pH 7', '5 mM sodium
|    bicarbonate buffer, pH 9', 'Gut saline medium'}
```

Class 'Continuous flow dissolution assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'ISO 19057:2017'	
assay_descriptor	: AssayDescriptor	'Continuous Flow System'	
abbreviation	: String	"CFS"	
minimum_tier	: TierLevel	TL1	*E-G-1*

Operators

```
function 'Continuous flow dissolution assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_WATER_SOL{EP_DISSOLUTION_RATE, EP_DISSOLUTION_HALF_TIME, EP_TRANSFORMATION_D1, EP_TRANSFORMATION_D3, EP_TRANSFORMATION_MORPHOLOGY}

function 'Continuous flow dissolution assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Simulated lung airway lining fluid', 'Simulated lung macrophage phagolysosomal fluid', 'Simulated saliva fluid', 'Simulated gastric fluid', 'Simulated intestinal fluid', 'Simulated saliva (5min) +
|     gastric fluid', 'Simulated saliva (5min) + gastric(2h) + intestinal fluid', 'Simulated sweat'} + MediumDescriptors{'OECD TG318 medium + NOM, pH 4', 'OECD TG318 medium + NOM, pH 7', 'OECD TG318 medium + NOM, pH
|    9', 'Relevant aquatic medium'}
```

Class 'Electrophoretic Light Scattering assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Electrophoretic Light Scattering'	
abbreviation	: String	"ELS"	

Operators

```
function 'Electrophoretic Light Scattering assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_ZETA_POTENTIAL{PC_ZETA_POTENTIAL::EP_ZETA_POTENTIAL, PC_ZETA_POTENTIAL::EP_ISOELECTRIC_POINT}
```

Class 'X-Ray Fluorescence assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'X-Ray Fluorescence'	
abbreviation	: String	"XRF"	

Class 'Thermogravimetric Analysis/Mass Spectrometry assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Thermogravimetric Analysis/Mass Spectrometry'	
abbreviation	: String	"TGA-MS"	

Operators

```
function 'Thermogravimetric Analysis/Mass Spectrometry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_STABILITY_THERMAL_SUNLIGHT_METALS{EP_MASS_LOSS, EP_MASS_LOSS_WATER}
```

Class 'Thermogravimetric Analysis assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Thermogravimetry'	
abbreviation	: String	"TGA"	

Operators

```
function 'Thermogravimetric Analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_AEROSOL_CHARACTERISATION::EP_AEROSOLISED_PARTICLE_CONC}
```

Class 'Inductively Coupled Plasma Optical Emission Spectrometry assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Inductively Coupled Plasma Optical Emission Spectrometry'	
abbreviation	: String	"ICP-OES"	

Operators

```
function 'Inductively Coupled Plasma Optical Emission Spectrometry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_COMPOSITION{EP_ELEMENTAL_COMPOSITION_MASS_CONC}
```

Class 'Multiple Path Particle Dosimetry assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Multiple Path Particle Dosimetry model'	
abbreviation	: String	"MPPD"	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Multiple Path Particle Dosimetry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  HH_LUNG_DEPOSITION{EP_DEPOSITION_FRACTION_TRACHEA_BRONCHI, EP_DEPOSITION_FRACTION_ALVEOLI}
```

Class 'Cascade Impactor Measurement assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Cascade Impactor Measurement'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Cascade Impactor Measurement assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_GRANULOMETRY::EP_AERODYNAMIC_EQ_SPHERE_DIAMETER, PC_GRANULOMETRY::EP_MASS_MEDIAN_AERODYNAMIC_DIAMETER}
```

Class 'Ferric reduction ability of serum assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Ferric Reduction Ability of Serum'	
abbreviation	: String	"FRAS"	

Operators

```
function 'Ferric reduction ability of serum assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_PER_DOSE, PC_RADICAL_FORMATION_POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_MASS_DOSE, EP_FRAS_SCORE_MASS, EP_FRAS_SCORE_SURF, PC_RADICAL_FORMATION_
     POTENTIAL::EP_BIOLOGICAL_OXIDATIVE_DAMAGE_SURF_DOSE, PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_SURFACE}

function 'Ferric reduction ability of serum assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Human blood serum (HBS)'}
```

Class 'Dichlorodihydrofluorescin diacetate assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Dichlorodihydrofluorescin diacetate'	
abbreviation	: String	"DCFH2-DA"	

Operators

```
function 'Dichlorodihydrofluorescin diacetate assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU, EP_DCFH_ROS_GENERATION_AU, PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_OXIDATION_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_SCORE_MASS, PC_
     RADICAL_FORMATION_POTENTIAL::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL, PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_INTRINSIC_ROS_CHANGE_IN_RFU} + Enumerates{HH_OXIDATIVE_STRESS::EP_DCFH_RFU_CHANGE, EP_DCFH_AIR_LIQUID_
     INTERFACE_PERC_OF_CONTROL, HH_OXIDATIVE_STRESS::EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL}
```

Class 'Electron Paramagnetic Resonance assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Electron Paramagnetic Resonance'	
abbreviation	: String	"EPR/ESR"	

Operators

```
function 'Electron Paramagnetic Resonance assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_RADICAL_FORMATION_POTENTIAL::EP_SPIN_COUNT_PER_SURFACE_CONC, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_
     SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_SURF, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_SURF, PC_RADICAL_
     FORMATION_POTENTIAL::EP_EPR_SCORE_MASS, PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY, EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL}

function 'Electron Paramagnetic Resonance assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2'}
```

Class 'Protein Carbonylation assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Protein Carbonylation Assay'	

Operators

```
function 'Protein Carbonylation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_OXIDATIVE_STRESS::EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN}

function 'Protein Carbonylation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Human blood serum (HBS)'}
```

Class 'Screening transformation/dissolution test assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 29'	
assay_descriptor	: AssayDescriptor	'Screening transformation/dissolution test - sparingly soluble metal compounds'	

Operators

```
function 'Screening transformation/dissolution test assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_WATER_SOL::EP_SOLUBILITY}
```

Class 'Batch dispersion quality assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Batch dispersion quality Assay'	

Operators

```
function 'Batch dispersion quality assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_GRANULOMETRY::EP_Z_AVERAGE_DIAMETER, PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER}
```

Class 'Water Solubility assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 105'	
assay_descriptor	: AssayDescriptor	'Water Solubility Assay'	

Operators

```
function 'Water Solubility assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_WATER_SOL::EP_WATER_SOL}
```

Class 'Energy-Dispersive X-ray Spectroscopy assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Energy-Dispersive X-ray Spectroscopy'	
abbreviation	: String	"EDX"	

Operators

```
function 'Energy-Dispersive X-ray Spectroscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC}
```

Class 'Isothermal Titration Calorimetry (ITC) assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Isothermal Titration Calorimetry Assay'	
abbreviation	: String	"ITC"	

Operators

```
function 'Isothermal Titration Calorimetry (ITC) assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_BIOMOL_INTERACTION::EP_BINDING_ENERGY, PC_BIOMOL_INTERACTION::EP_BINDING_ENTHALPY, PC_BIOMOL_INTERACTION::EP_BINDING_ENTROPY}
```

Class 'Centrifugal Liquid Sedimentation assay' is kind of PC_Assay

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Centrifugal Liquid Sedimentation'	
abbreviation	: String	"CLS"	

Operators

```
function 'Centrifugal Liquid Sedimentation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_GRANULOMETRY::EP_DmPx_D1}

function 'Centrifugal Liquid Sedimentation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Simulated intestinal fluid'}
```

Class `'Evolved-Gas Analysis assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Evolved-Gas Analysis'	
abbreviation	: String	"EGA"	

Operators

```
function 'Evolved-Gas Analysis assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC}
```

Class `'Tunable Resistive Pulse Sensing assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Tunable Resistive Pulse Sensing'	
abbreviation	: String	"TRPS"	

Operators

```
function 'Tunable Resistive Pulse Sensing assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_ZETA_POTENTIAL::EP_ZETA_POTENTIAL}
```

Class `'Atomic Force Microscopy assay'` is kind of `PC_Assay`

Assays to estimate or measure physical or chemical properties of a substance.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Atomic Force Microscopy'	
abbreviation	: String	"AFM"	

Operators

```
function 'Atomic Force Microscopy assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_GRANULOMETRY::EP_DnPx_D1, PC_GRANULOMETRY::EP_DnPx_D3}

function 'Atomic Force Microscopy assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'Sterile filtered water', 'Simulated sweat'}
```

Class `EN_Assay` is kind of `Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	

Class `'Screening dispersion assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 318'	
assay_descriptor	: AssayDescriptor	'Screening dispersion Assay'	

Operators

```
function 'Screening dispersion assay'.ResultEndpointDomain(): Enumerates [specialization]
|  EN_DISPERSION_STABILITY_NANOMATERIAL{EP_DISPERSION_STABILITY}
```

```
function 'Screening dispersion assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)', 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)', 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)'}
```

Class `'Screening batch retention assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Screening batch retention Test'	

Operators

```
function 'Screening batch retention assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_DISPERSION_STABILITY_NANOMATERIAL::EP_BATCH_RETENTION_COEFFICIENT}
```

```
function 'Screening batch retention assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  Enumerates{'0.01 mM CaCl2'}
```

Class `'Screening heteroaggregation dispersion assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Screening heteroaggregation dispersion Assay '	

Operators

```
function 'Screening heteroaggregation dispersion assay'.ResultEndpointDomain(): Enumerates [specialization]
|  EN_DISPERSION_STABILITY_NANOMATERIAL{EP_DISPERSION_STABILITY}
```

Class `'Extended dispersion assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 318'	
assay_descriptor	: AssayDescriptor	'Extended dispersion Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Extended dispersion assay'.ResultEndpointDomain(): Enumerates [specialization]
|  EN_DISPERSION_STABILITY_NANOMATERIAL{EP_DISPERSION_STABILITY}

function 'Extended dispersion assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 4)', 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 7)', 'OECD TG318 medium + NOM (0,1, 10 Ca(NO3)2, pH 9)', 'OECD TG318 medium + no NOM (0,1, 10 Ca(
|     NO3)2, pH 4)', 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 7)', 'OECD TG318 medium + no NOM (0,1, 10 Ca(NO3)2, pH 9)', 'Relevant aquatic medium'}
```

Class `'Macrophage-assisted dissolution assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Macrophage-assisted dissolution Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Macrophage-assisted dissolution assay'.ResultEndpointDomain(): Enumerates [specialization]
|  PC_WATER_SOL{EP_INTRACELLULAR_DISSOLUTION_MASS_LOSS, EP_INTRACELLULAR_DISSOLUTION_HALF_TIME, EP_INTRACELLULAR_DISSOLUTION_RATE}

function 'Macrophage-assisted dissolution assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Cell culture medium, pH 7.4'}

function 'Macrophage-assisted dissolution assay'.CellDescriptorDomain(): Enumerates [specialization]
|  CellLineDescriptor{'NR8383 (rat alveolar macrophages cell line)'}
```

Class `'Nanomaterial removal in waste water assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD WNT 3.11'	
assay_descriptor	: AssayDescriptor	'Nanomaterial removal in wastewater Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Nanomaterial removal in waste water assay'.ResultEndpointDomain(): Enumerates [specialization]
|  EN_DISPERSION_STABILITY_NANOMATERIAL{EP_DISPERSION_STABILITY}
```

```
function 'Nanomaterial removal in waste water assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Simulated waste water'}
```

Class 'Biodegradation MT2 screen assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Biodegradation MT-2 screening Assay'	

Operators

```
function 'Biodegradation MT2 screen assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}
```

```
function 'Biodegradation MT2 screen assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class 'Biodegradation DOC Die-Away assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-A'	
assay_descriptor	: AssayDescriptor	'Biodegradation DOC Die-Away Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation DOC Die-Away assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}
```

```
function 'Biodegradation DOC Die-Away assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class 'Biodegradation CO2 Evolution assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-B'	
assay_descriptor	: AssayDescriptor	'Biodegradation CO2 Evolution Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation CO2 Evolution assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}
```

```
function 'Biodegradation CO2 Evolution assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class 'Biodegradation MITI (I) assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-C'	
assay_descriptor	: AssayDescriptor	'Biodegradation MITI (I) Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation MITI (I) assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}
```

```
function 'Biodegradation MITI (I) assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class 'Biodegradation Closed Bottle assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-E'	
assay_descriptor	: AssayDescriptor	'Biodegradation Closed Bottle Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation Closed Bottle assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}

function 'Biodegradation Closed Bottle assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class `'Biodegradation Modified OECD Screening assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-D'	
assay_descriptor	: AssayDescriptor	'Biodegradation Modified OECD screening Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation Modified OECD Screening assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}

function 'Biodegradation Modified OECD Screening assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class `'Biodegradation Manometric Respirometry assay'` is kind of `EN_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 301-F'	
assay_descriptor	: AssayDescriptor	'Biodegradation Manometric Respirometry Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Biodegradation Manometric Respirometry assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SCREEN::EP_PERCENT_BIODEG}

function 'Biodegradation Manometric Respirometry assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'OECD TG301 mineral medium'}
```

Class `'Biodegradation Aerobic sewage assay'` is kind of `EN_Assay`

TO DO E-G-4

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 303-A'	
assay_descriptor	: AssayDescriptor	'Biodegradation Aerobic sewage Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Biodegradation Aerobic sewage assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Biodegradation waste water discharge, sewer system assay' is kind of EN_Assay

TO BE SPLIT INTO SEPARATE ASSAYS A..E with each different medium desciptor

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 314-A'	
assay_descriptor	: AssayDescriptor	'Biodegradation wastewater discharge, sewer systems Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Biodegradation waste water discharge, sewer system assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Biodegradation waste water discharge, activated sludge assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 314-B'	
assay_descriptor	: AssayDescriptor	'Biodegradation wastewater discharge, activated sludge Assay'	

Operators

```
function 'Biodegradation waste water discharge, activated sludge assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Biodegradation wastewater discharge, anaerobic digester sludge assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 314-C'	
assay_descriptor	: AssayDescriptor	'Biodegradation wastewater discharge, anaerobic digester sludge'	

Operators

```
function 'Biodegradation wastewater discharge, anaerobic digester sludge assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Biodegradation wastewater discharge, treated effluent in the mixing zone of surface water assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 314-D'	
assay_descriptor	: AssayDescriptor	'Biodegradation wastewater discharge, treated effluent in the mixing zone of surface water'	

Operators

```
function 'Biodegradation wastewater discharge, treated effluent in the mixing zone of surface water assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Biodegradation wastewater discharge, untreated wastewater that is directly discharged to surface water assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 314-E'	
assay_descriptor	: AssayDescriptor	'Biodegradation wastewater discharge, untreated wastewater that is directly discharged to surface water'	

Operators

```
function 'Biodegradation wastewater discharge, untreated wastewater that is directly discharged to surface water assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_WATER_SIM::EP_PERCENT_BIODEG}
```

Class 'Direct photolysis theoretical screen assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 316'	
assay_descriptor	: AssayDescriptor	'Direct photolysis theroretical screening Assay'	

Operators

```
function 'Direct photolysis theoretical screen assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_PHOTOTRANS_WATER::EP_PHOTOLYSIS_HALF_TIME}
```

Class 'Direct photolysis aquatic assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 316'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Direct photolysis aquatic assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_PHOTOTRANS_WATER::EP_PHOTOLYSIS_HALF_TIME}

function 'Direct photolysis aquatic assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Buffered pure water'}
```

Class 'Inherent biodegradability in soil assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 304-A'	
assay_descriptor	: AssayDescriptor	'Inherent biodegradability in soil Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Inherent biodegradability in soil assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_SOIL::EP_PERCENT_BIODEG}

function 'Inherent biodegradability in soil assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Relevant soil medium'}
```

Class 'Aerobic soil transformation assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 307'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Aerobic soil transformation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_BIODEG_SOIL::EP_PERCENT_BIODEG}
```

```
function 'Aerobic soil transformation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Relevant soil medium'}
```

Class 'Photodegradation at soil surface assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'GSD N 161-3'	

Operators

```
function 'Photodegradation at soil surface assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_PHOTOTRANS_SOIL::EP_PHOTOLYSIS_HALF_TIME}
```

```
function 'Photodegradation at soil surface assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Relevant soil medium'}
```

Class 'DLVO attachment efficiency derivation assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'DLVO attachment efficiency derivation method'	

Operators

```
function 'DLVO attachment efficiency derivation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EN_DISPERSION_STABILITY_NANOMATERIAL::EP_DISPERSION_STABILITY}
```

```
function 'DLVO attachment efficiency derivation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'SimpleBox4nano freshwater'}
```

Class 'Column leaching assay' is kind of EN_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'OECD 312'	
assay_descriptor	: AssayDescriptor	'Column leaching Test'	

Class `HH_Assay` is kind of `Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Class `'Cascade in vitro digestion assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Cascade in vitro digestion Assay'	

Class `'In Vivo Mammalian Alkaline COMET assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 489'	
assay_descriptor	: AssayDescriptor	'In Vivo Mammalian Alkaline COMET Assay'	
abbreviation	: String	"COMET"	

Operators

```
function 'In Vivo Mammalian Alkaline COMET assay'.ResultEndpointDomain(): Enumerates [specialization]
| Enumerates{HH_GENETIC_IN_VIVO::EP_DNA_STRAND_BREAKS, HH_GENETIC_IN_VITRO::EP_DNA_STRAND_BREAKS, HH_GENETIC_IN_VITRO::EP_FPG_SENSITIVE_SITES}
```

Class `'LDH assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Lactate DeHydrogenase Assay'	
abbreviation	: String	"LDH"	

Operators

```
function 'LDH assay'.ResultEndpointDomain(): Enumerates [specialization]
| Enumerates{HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL, HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE}
```

Class `'Alamar Blue assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Alamar Blue Metabolic Cell Viability Assay'	
abbreviation	: String	"Alamar Blue"	

Operators

```
function 'Alamar Blue assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE, EC_FISH_TOX_SHORT::EP_METABOLIC_ACTIVITY}
```

Class 'WST-1 assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'WST-1 Metabolic Cell Viability Assay'	
abbreviation	: String	"WST-1"	

Operators

```
function 'WST-1 assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_450_NM, HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_
    NM}
```

Class 'WST-8 assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'WST-8 Metabolic Cell Viability Assay'	
abbreviation	: String	"WST-8"	

Operators

```
function 'WST-8 assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_CELL_VIABILITY, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_450_NM, HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_
    NM}
```

Class 'In vivo intratracheal instillation assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 39'	*Lung burden OECD GD39*
assay_descriptor	: AssayDescriptor	'In vivo intratracheal instillation Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'In vivo intratracheal instillation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_LUNG_INSTILLATION::EP_RETAINED_FIBRE_BURDEN, EP_RETAINED_FIBRE_HALF_TIME}

function 'In vivo intratracheal instillation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'In vivo dispersion media'}
```

Class 'Short Term Inhalation Study assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Short Term Inhalation Study'	
abbreviation	: String	"STIS"	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Short Term Inhalation Study assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_TOX_CATEGORY_STIS, HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx, HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_TIME, HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE}
```

Class 'Subacute Inhalation Toxicity assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 412'	*Lung burden OECD TG412, OECD GD39*
assay_descriptor	: AssayDescriptor	'Subacute Inhalation Toxicity Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Subacute Inhalation Toxicity assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_LUNG_INSTILLATION::EP_RETAINED_FIBRE_BURDEN, EP_RETAINED_FIBRE_HALF_TIME, HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx, HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_TIME, HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE}
```

Class 'Subchronic Inhalation Toxicity assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 413'	
assay_descriptor	: AssayDescriptor	'Subchronic Inhalation Toxicity Assay'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Subchronic Inhalation Toxicity assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_LUNG_INSTILLATION::EP_RETAINED_FIBRE_BURDEN, EP_RETAINED_FIBRE_HALF_TIME, HH_LUNG_INSTILLATION::EP_LUNG_BURDEN_Tx, HH_LUNG_INSTILLATION::EP_IN_VIVO_HALF_TIME, HH_LUNG_INSTILLATION::EP_CLEARANCE_RATE}
```

Class 'In vitro biological stiffness assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'In vitro biological stiffness Assay'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'In vitro biological stiffness assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{PC_RIGIDITY::EP_BIOLOGICAL_STIFFNESS}
```

Class 'Inflammasome activation assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Inflammasome activation'	

Operators

```
function 'Inflammasome activation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_INFLAMMATION::EP_INFLAMMASOME, HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE}

function 'Inflammasome activation assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Cell culture medium, RPMI supplemented with 1% pen/strep, 10% FBS, 1% L-glutamine'}

function 'Inflammasome activation assay'.CellDescriptorDomain(): Enumerates [specialization]
|  CellLineDescriptor{'THP-1 (human leukemic monocyte cell line)'}
```

Class 'In vitro alveolar macrophage assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'In vitro alveolar macrophage Assay'	

Class 'Enzyme-Linked Immunosorbent assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Enzyme-Linked Immunosorbent Assay'	
abbreviation	: String	"ELISA"	

Operators

```
function 'Enzyme-Linked Immunosorbent assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE, HH_IMMUNOTOXICITY::EP_HEAT_SHOCK_PROTEIN_PERC_OF_CONTROL}
```

Class `'Nrf2 activation assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'NRF2 Activation Assay'	
abbreviation	: String	"NRF2"	

Operators

```
function 'Nrf2 activation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_NRF2_LUCIFERASE_ACTIVITY, EP_NRF2_FOLD_LUCIFERASE_ACTIVITY_INDUCTION}

function 'Nrf2 activation assay'.CellDescriptorDomain(): Enumerates [specialization]
|  Enumerates{'HEK293 (human embryonic kidney cell line)'}
```

Class `'Neutral Red Uptake Cell Viability assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Neutral Red Uptake Cell Viability Assay'	
abbreviation	: String	"NRU"	

Operators

```
function 'Neutral Red Uptake Cell Viability assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_NRU_VIABILITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM, EC_FISH_TOX_SHORT::EP_LYSOSOMAL_INTEGRITY}
```

Class `'Repeated Dose 90-Day Oral Toxicity Study in Rodents assay'` is kind of `HH_Assay`

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 408'	
assay_descriptor	: AssayDescriptor	'Repeated Dose 90-Day Oral Toxicity Study in Rodents'	
minimum_tier	: TierLevel	TL3	

Operators

```
function 'Repeated Dose 90-Day Oral Toxicity Study in Rodents assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_REPEATED_ORAL::EP_CELL_NUMBER_IN_BALF, EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_PERC_IN_BALF, HH_REPEATED_
   ORAL::EP_ALVEOLAR_LYMPHOCYTES_PERC_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_NUMBER_IN_
   BALF, HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_NUMBER_IN_BALF}
```

Class 'Consecutive in vitro digestion assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Consecutive in vitro digestion Assay'	

Operators

```
function 'Consecutive in vitro digestion assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_PERCENTAGE_DISSOLVED}

function 'Consecutive in vitro digestion assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptors{'Simulated saliva fluid', 'Simulated gastric fluid', 'Simulated intestinal fluid', 'Simulated saliva (5min) + gastric fluid', 'Simulated saliva (5min) + gastric(2h) + intestinal fluid'}
```

Class 'Cytokinesis Block Micronucleus Cytome assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Cytokinesis Block Micronucleus Cytome Assay'	
abbreviation	: String	"CBMN"	

Class 'In vitro granuloma formation assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'In vitro granuloma formation Assay'	

Operators

```
function 'In vitro granuloma formation assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_IN_VITRO_GRANULOMA_FORMATION}

function 'In vitro granuloma formation assay'.CellDescriptorDomain(): Enumerates [specialization]
|  Enumerates{'Macrophages'}
```

Class 'MTS cell viability assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'MTS Cell Viability Assay'	
abbreviation	: String	"MTS"	

Operators

```
function 'MTS cell viability assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL}
```

```
function 'MTS cell viability assay'.CellDescriptorDomain(): Enumerates [specialization]
|  Enumerates{'CACO-2 (human cell line)'}
```

Class 'TransEpithelial Electrical Resistance assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'TransEpithelial Electrical Resistance Assay'	
abbreviation	: String	"TEER"	

Operators

```
function 'TransEpithelial Electrical Resistance assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EP_INVITRO_BARRIER_INTEGRITY, EP_TEER_DECREASE_VERSUS_CONTROL}
```

```
function 'TransEpithelial Electrical Resistance assay'.CellDescriptorDomain(): Enumerates [specialization]
|  Enumerates{'CACO-2 (human cell line)'}
```

Class 'In Vitro Mammalian Cell Gene Mutation assay using the Hprt and xprt genes' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 476'	
assay_descriptor	: AssayDescriptor	'In Vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes'	

Class 'In Vitro Mammalian Cell Gene Mutation assay using the Thymidine Kinase Gene' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 490'	
assay_descriptor	: AssayDescriptor	'In Vitro Mammalian Cell Gene Mutation Tests using the Thymidine Kinase Gene'	

Class 'Glutathione assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Glutathione Assay'	
abbreviation	: String	"GSH"	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Glutathione assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_OXIDATIVE_STRESS::EP_CHANGE_IN_GSH_LEVEL, HH_OXIDATIVE_STRESS::EP_IN_VITRO_GHS_OXIDATIVE_STRESS_QUANTIFICATION}
```

Class 'Lipid Peroxidation (MDA) assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Lipid Peroxidation (MDA) Assay'	
abbreviation	: String	"MDA"	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Lipid Peroxidation (MDA) assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_OXIDATIVE_STRESS::EP_MDA_LIPID_PEROXIDATION}
```

Class 'LUMINEX assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'LUMINEX Assay'	

Operators

```
function 'LUMINEX assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_IMMUNOTOXICITY::EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION}
```

Class 'Lucifer Yellow assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Lucifer Yellow Assay'	

Class 'Resazurin Metabolic Cell Viability assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Resazurin Metabolic Cell Viability Assay'	
abbreviation	: String	"RESAZURIN"	

Operators

```
function 'Resazurin Metabolic Cell Viability assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_RESAZURIN_VIABILITY_PERC_OF_CONTROL}
```

Class 'Impedance Analysis of Adherent Cells assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Impedance Analysis of Adherent Cells'	

Operators

```
function 'Impedance Analysis of Adherent Cells assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_NORMALISED_POST_EXPOSURE_CELL_INDEX_1, HH_CYTOTOXICITY::EP_IAAC_CYTOTOXICITY_PERC_OF_CONTROL, HH_CYTOTOXICITY::EP_IAAC_CYTOTOXICITY_ICx}
```

Class 'May-Grunwald Giemsa coloration of BAL cells cytospin assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'May-Grunwald Giemsa coloration of BAL cells cytospin'	
abbreviation	: String	"MGG"	

Operators

```
function 'May-Grunwald Giemsa coloration of BAL cells cytospin assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF, HH_REPEATED_INHAL::EP_ALVEOLAR_
   NEUTROPHILS_NUMBER_IN_BALF}
```

Class 'CFDA-AM assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'CFDA-AM Assay'	
abbreviation	: String	"CFDA-AM"	*CFDA-AM based on 5-carboxyfluorescein diacetate acetoxymethyl ester*

Operators

```
function 'CFDA-AM assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_SHORT::EP_PLASMA_MEMBRANE_INTEGRITY}
```

Class 'Colony Forming Efficiency assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Colony Forming Efficiency Assay'	
abbreviation	: String	"CFE"	

Operators

```
function 'Colony Forming Efficiency assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_CYTOTOXICITY::EP_CFE_CYTOTOXICITY_PERC_OF_CONTROL}
```

Class 'In vivo oral toxicokinetic study' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 417'	
assay_descriptor	: AssayDescriptor	'In vivo oral toxicokinetic Study'	

Operators

```
function 'In vivo oral toxicokinetic study'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_BASIC_TOX::EP_IN_VIVO_ACCUMULATION}
```

Class 'Heme Oxygenase 1 assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Heme Oxygenase 1 Assay'	
abbreviation	: String	"HMOX"	

Operators

```
function 'Heme Oxygenase 1 assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_OXIDATIVE_STRESS::EP_IN_VITRO_HMOX_OXIDATIVE_STRESS_NFOLD_NEG_CONTROL}
```

Class 'Microbiota cell wall integrity assay' is kind of HH_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
assay_descriptor	: AssayDescriptor	'Microbiota cell wall integrity Assay'	

Operators

```
function 'Microbiota cell wall integrity assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{HH_BARRIER_INTEGRITY::EP_IN_VITRO_INTESTINAL_MICROBIOTA_INTEGRITY}
```

Class EC_Assay is kind of Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Class 'Enchytraeid reproduction test' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 220'	

Operators

```
function 'Enchytraeid reproduction test'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SOIL_TOX::EP_SURVIVAL, EC_SOIL_TOX::EP_REPRODUCTION}
```

Class 'Acute toxicity test with algae' is kind of EC_Assay

Freshwater Alga and Cyanobacteria, Growth Inhibition Test (OECD 201)

Defined expressions

name	type	expression	comment
title	: String	"Freshwater Alga and Cyanobacteria, Growth Inhibition Test"	
guideline	: any Enumerate	'OECD 201'	
assay_descriptor	: AssayDescriptor	'Freshwater Alga **and** Cyanobacteria, Growth Inhibition Test'	

Operators

```
function 'Acute toxicity test with algae'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_ALGAE_TOX::EP_GROWTH, EC_ALGAE_TOX::EP_BIOMASS, EC_ALGAE_TOX::EP_YIELD}
```

Class 'Acute toxicity test with daphnids' is kind of EC_Assay

Daphnia sp. Acute Immobilisation Test (OECD 202)

Defined expressions

name	type	expression	comment
title	: String	"Daphnia sp. Acute Immobilisation Test"	
guideline	: any Enumerate	'OECD 202'	
assay_descriptor	: AssayDescriptor	'Daphnia sp. Acute Immobilisation Test'	

Operators

```
function 'Acute toxicity test with daphnids'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION, EC_AQUATIC_INVERT_TOX_SHORT::EP_MORTALITY}
```

Class 'Fish, Early-Life Stage Toxicity Test Assay' is kind of EC_Assay

Fish, Early-life Stage Toxicity Test (OECD 210)

Defined expressions

name	type	expression	comment
title	: String	"Fish, Early-life Stage Toxicity Test"	
guideline	: any Enumerate	'OECD 210'	
assay_descriptor	: AssayDescriptor	'Fish, Early-life Stage Toxicity Test'	

Operators

```
function 'Fish, Early-Life Stage Toxicity Test Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_CHRONIC::EP_MORTALITY, EC_FISH_TOX_CHRONIC::EP_DEVELOPMENT, EC_FISH_TOX_CHRONIC::EP_SURVIVAL, EC_FISH_TOX_CHRONIC::EP_HATCHING, EC_FISH_TOX_CHRONIC::EP_WEIGHT, EC_FISH_TOX_CHRONIC::EP_
     LENGTH, EC_FISH_TOX_CHRONIC::EP_ABNORMAL_APPEARANCE_AND_BEHAVIOR}
```

Class 'Acute toxicity test with fish embryos' is kind of EC_Assay

Fish Embryo Acute Toxicity (FET) Test (OECD 236)

Defined expressions

name	type	expression	comment
title	: String	"Acute toxicity test with fish embryos"	
guideline	: any Enumerate	'OECD 236'	
assay_descriptor	: AssayDescriptor	'Fish embryo acute toxicity (FET) test'	

Operators

```
function 'Acute toxicity test with fish embryos'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_SHORT::EP_COAGULATION_OF_FERTILISED_EGGS, EC_FISH_TOX_SHORT::EP_LACK_OF_SOMITE_FORMATION, EC_FISH_TOX_SHORT::EP_LACK_OF_DETACHMENT_OF_TAIL_BUD_FROM_YOLK_SAC, EC_FISH_TOX_SHORT::EP_LACK_OF_
    HEARTBEAT, EC_FISH_TOX_SHORT::EP_MORTALITY}
```

Class 'Chronic toxicity test with daphnids' is kind of EC_Assay

Daphnia magna Reproduction Test (OECD 211)

Defined expressions

name	type	expression	comment
title	: String	"Daphnia magna Reproduction Test"	
guideline	: any Enumerate	'OECD 211'	
assay_descriptor	: AssayDescriptor	'Daphnia magna Reproduction Test'	

Operators

```
function 'Chronic toxicity test with daphnids'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_AQUATIC_INVERT_TOX_CHRONIC::EP_REPRODUCTION, EC_AQUATIC_INVERT_TOX_CHRONIC::EP_IMMOBILIZATION}
```

Class 'Acute toxicity test with Chironomus' is kind of EC_Assay

"Chironomus sp., Acute Immobilisation Test"

Defined expressions

name	type	expression	comment
title	: String	"Chironomus sp. Acute Immobilisation Test"	
guideline	: any Enumerate	'OECD 235'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Acute toxicity test with Chironomus'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION, EC_AQUATIC_INVERT_TOX_SHORT::EP_GROWTH}
```

Class 'Acute toxicity test with fish (TL2)' is kind of EC_Assay

Fish, Acute Toxicity Test (OECD 203)

Defined expressions

name	type	expression	comment
title	: String	"Fish, Acute Toxicity Testing"	
guideline	: any Enumerate	'OECD 203'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Acute toxicity test with fish (TL2)'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_SHORT::EP_MORTALITY}
```

Class 'Sub-chronic toxicity test with water plants' is kind of EC_Assay

Lemna sp. Growth Inhibition Test (OECD 221)

Defined expressions

name	type	expression	comment
title	: String	"Lemna sp. Growth Inhibition Test"	
guideline	: any Enumerate	'OECD 221'	
minimum_tier	: TierLevel	TL2	

Operators

```
function 'Sub-chronic toxicity test with water plants'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_AQ_PLANTS_NONE_ALGAE::EP_GROWTH, EC_AQ_PLANTS_NONE_ALGAE::EP_YIELD}
```

Class 'Fish Short Term Reproduction Assay' is kind of EC_Assay

Fish Short Term Reproduction Assay (OECD 229)
()

Defined expressions

name	type	expression	comment
title	: String	"Fish Short Term Reproduction Assay"	
guideline	: any Enumerate	'OECD 229'	
actual_tier	: TierLevel	TL3	

Operators

```
function 'Fish Short Term Reproduction Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_CHRONIC::EP_GROWTH}
```

Class 'Chronic toxicity test with fish 2' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'OECD 204'	

Class 'Short Term Screening 21-day Fish Assay' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
title	: String	"21-day Fish Assay - A Short-Term Screening for Oestrogenic and Androgenic Activity, and Aromatase Inhibition"	
guideline	: any Enumerate	'OECD 230'	

Operators

```
function 'Short Term Screening 21-day Fish Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_FISH_TOX_CHRONIC::EP_MORTALITY}
```

Class 'Caenorhabditis elegans sediment toxicity Assay' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'ISO 10872:2020'	
assay_descriptor	: AssayDescriptor	'Caenorhabditis elegans sediment toxicity test'	

Operators

```
function 'Caenorhabditis elegans sediment toxicity Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION}

function 'Caenorhabditis elegans sediment toxicity Assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptor{'M9 medium', 'ISO artificial sediment'}
```

Class 'Water-sediment Myriophyllum spicantum toxicity Assay' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'OECD 239'	
assay_descriptor	: AssayDescriptor	'Water-sediment Myriophyllum spicantum toxicity test'	

Operators

```
function 'Water-sediment Myriophyllum spicantum toxicity Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION}
```

```
function 'Water-sediment Myriophyllum spicantum toxicity Assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptor{'OECD 219 sediment', 'Smart and Barko medium'}
```

Class 'Sediment-water Lumbriculus toxicity test using spiked sediment Assay' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'OECD 225'	
assay_descriptor	: AssayDescriptor	'Sediment-water Lumbriculus toxicity test using spiked sediment'	

Operators

```
function 'Sediment-water Lumbriculus toxicity test using spiked sediment Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION, EC_SEDIMENT_TOX::EP_SURVIVAL}
```

```
function 'Sediment-water Lumbriculus toxicity test using spiked sediment Assay'.MediumDescriptorDomain(): MediumDescriptors [specialization]
|  MediumDescriptor{'OECD 203 water', 'OECD 225 sediment'}
```

Class 'Sediment-water Chironomid spiked sediment toxicity Assay'' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Sediment-water Chironomid spiked sediment toxicity test'	

Operators

```
function 'Sediment-water Chironomid spiked sediment toxicity Assay''.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_EMERGENCE, EC_SEDIMENT_TOX::EP_DEVELOPMENT, EC_SEDIMENT_TOX::EP_DEVELOPMENT_RATE, EC_SEDIMENT_TOX::EP_SEX_RATIO, EC_SEDIMENT_TOX::EP_REPRODUCTION}
```

Class 'Leptocherius plumulosus chronic marine and estuarine sediment toxicity Assay' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
assay_descriptor	: AssayDescriptor	'Leptocherius plumulosus chronic marine and estuarine sediment toxicity test'	

Operators

```
function 'Leptocherius plumulosus chronic marine and estuarine sediment toxicity Assay'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_SURVIVAL, EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION}
```

Class 'Simulated freshwater lentic field Test' is kind of EC_Assay

An abstract class to derive classes from which can contain endpoints. For instance, Assay, Material, Chemical etc.

Defined expressions

name	type	expression	comment
medium_specific	: Boolean	True	
guideline	: any Enumerate	'OECD 53'	
assay_descriptor	: AssayDescriptor	'Simulated freshwater lentic field test'	

Operators

```
function 'Simulated freshwater lentic field Test'.ResultEndpointDomain(): Enumerates [specialization]
|  Enumerates{EC_SEDIMENT_TOX::EP_SURVIVAL, EC_SEDIMENT_TOX::EP_GROWTH, EC_SEDIMENT_TOX::EP_REPRODUCTION}
```

Class RE_Assay is kind of Assay

Assay for Release and Exposure

Class 'Mechanical machining assay' is kind of RE_Assay

Assay for Release and Exposure

Class 'Shredding assay' is kind of RE_Assay

Assay for Release and Exposure

Class 'Weathering assay' is kind of RE_Assay

Assay for Release and Exposure

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'ISO 4892-2'	

Class 'Crockmeter (JBA 302) assay' is kind of RE_Assay

Assay for Release and Exposure

Class 'Leaching assay' is kind of RE_Assay

Leaching (EPA Method 1311)

Defined expressions

name	type	expression	comment
guideline	: any Enumerate	'SW-846.1311'	

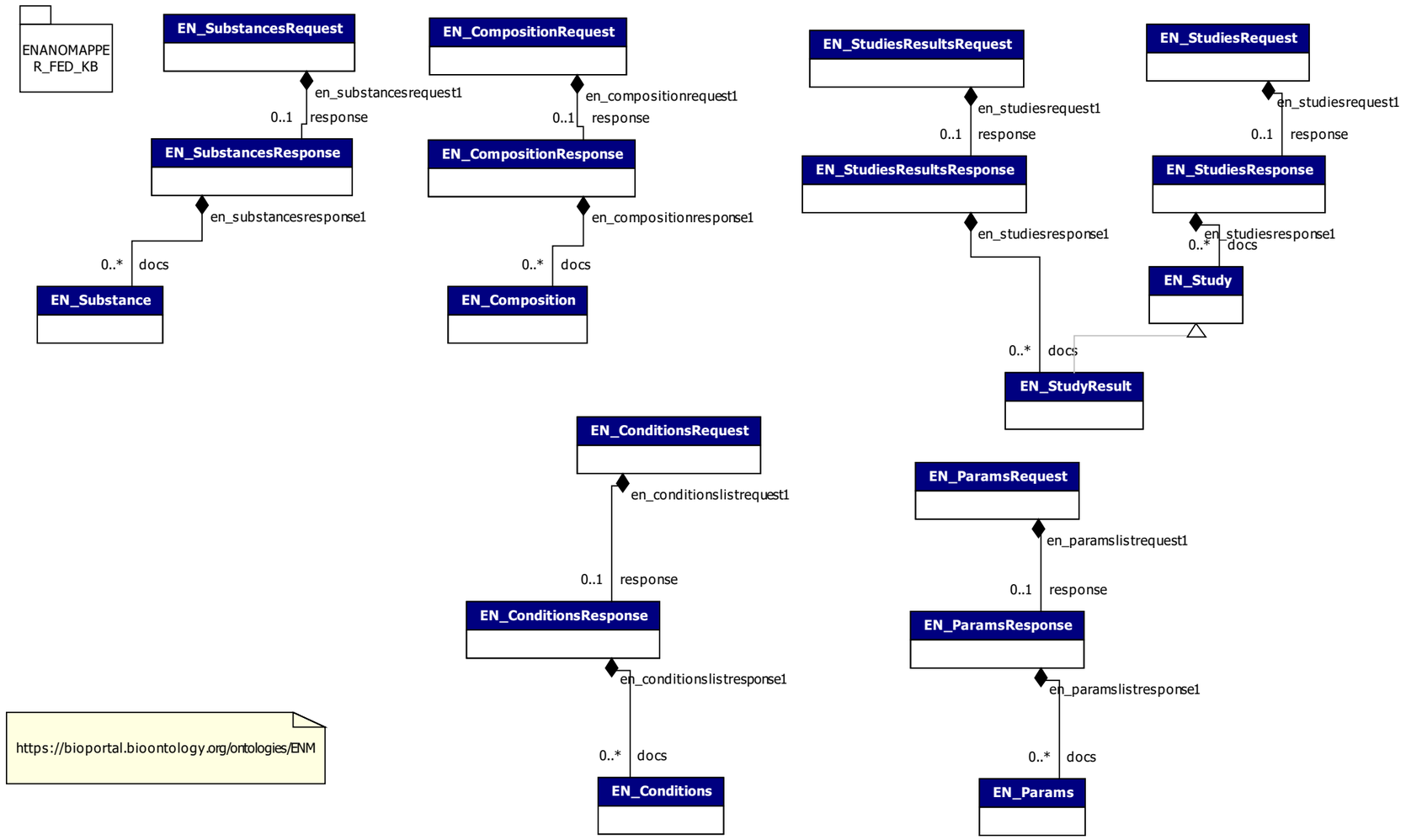
Class 'Incineration assay' is kind of RE_Assay

Assay for Release and Exposure

7.3 Defined collections

AssayClasses defines a sequence containing any kind of Assay types.
Assays defines a sequence containing any kind of Assay objects.
Ordered set AssayDescriptors
MediumDescriptors defines a sequence containing MediumDescriptor enumerates.

Chapter 8 ENANOMAPPER_FED_KB



https://search.data.enanomapper.net/gracious

8.1 Defined classes

Class `EN_SubstancesRequest`

Defined composites

Any instance of `EN_SubstancesRequest` is composed of
- at most one `response` of EN_SubstancesResponse

Class `EN_SubstancesResponse`

Defined composites

Any instance of `EN_SubstancesResponse` is composed of
- zero or more `docs` of EN_Substance

Class EN_Substance

Attributes

name	type	domain	inference	comment
dbtag_hss	: Strings			
name_hs	: String			
publicname_hs	: String			
owner_name_hs	: String			
content_hss	: String			
substanceType_hs	: String			
s_uuid_hs	: String			
type_s	: String			
nmcode_hs	: String			
substance_annotation_hss	: Strings			
'SUMMARY.SIZE_hss'	: Strings			
'SUMMARY.RESULTS_hss'	: Strings			
'SUMMARY.REFS_hss'	: Strings			
'SUMMARY.REFOWNERS_hss'	: Strings			
id	: String			
version	: Integer			

Class EN_CompositionRequest

Defined composites

Any instance of EN_CompositionRequest is composed of
- at most one response of EN_CompositionResponse

Class EN_CompositionResponse

Defined composites

Any instance of EN_CompositionResponse is composed of
- zero or more docs of EN_Composition

Class `EN_Composition`

Attributes

name	type	domain	inference	comment
`id`	: `String`			
`s_uuid_hs`	: `String`			
`type_s`	: `String`			
`component_s`	: `String`			
`ChemicalName_s`	: `String`			
`CASRN_s`	: `String`			
`EINECS_s`	: `String`			
`InChIKey_s`	: `String`			
`InChI_s`	: `String`			
`SMILES_s`	: `String`			
`_version_`	: `Integer`			

Class `EN_StudiesResultsRequest`

Defined composites

Any instance of `EN_StudiesResultsRequest` is composed of
- at most one `response` of `EN_StudiesResultsResponse`

Class `EN_StudiesResultsResponse`

Defined composites

Any instance of `EN_StudiesResultsResponse` is composed of
- zero or more `docs` of `EN_StudyResult`

Class `EN_Study`

Attributes

name	type	domain	inference	comment
`document_uuid_s`	: `String`			*Unique id for this study.*
`s_uuid_s`	: `String`			*The substance id this study is related to.*
`topcategory_s`	: `String`			*Domain {ECOTOX,P-CHEM,TOX}*
`'E.method_s'`	: `String`			
`guidance_s`	: `String`			
`guidance_synonym_ss`	: `Strings`			
`'E.method_synonym_ss'`	: `Strings`			

Operators

```
function EN_Study.DirectlyProvided(): Boolean
|  False
```

```
function EN_Study.MapTo_AssayDescriptors( p : EN_Params ): AssayDescriptors
  begin
    /* Tries to map an eNanoMapper study onto a GRACIOUS assay descriptor */  ;
    result→Add('Map E.method_s onto AssayDescriptor'(p));
    result→Add('Map guidance_s onto AssayDescriptor'(p));
    foreach syn of 'E.method_synonym_ss' do
    begin
      result→Add('Map ontology entry onto AssayDescriptor'(syn, p))
    end;
    foreach syn of guidance_synonym_ss do
    begin
      result→Add('Map ontology entry onto AssayDescriptor'(syn, p))
    end;
    result := result→Select(en | en ≠ nil)
  end
```

```
function EN_Study.'Map E.method_s onto AssayDescriptor'(p : EN_Params ): AssayDescriptor
  begin
    /* Tries to map an eNanoMapper study field E.method_s onto a GRACIOUS assay descriptor */  ;
    with 'Map abbreviation onto AssayDescriptor'('E.method_s') | assay_descriptor then
      result := assay_descriptor
    else
      case 'E.method_s' of
        "Aerosol Characterisation":
          begin
            /* Nanoreg, params indicate use of TGA testing used, release of nps on thermal degradation */          ;
            if p ≠ nil then
            begin
              case p.'T.AEROSOLISATION_METHOD_s' of
                "thermal degradation":
                  result := 'Thermogravimetry'
              end
            end
          end;
        "VSSA":
          begin
            /* Nanoreg, VSSA is wrong method name, should be SSA or better SBET */          ;
            result := 'Brunauer-Emmett-Teller method'
          end;
        "dustiness-small drum":
          result := 'Small rotating Drum';
        "Vortex Shaker":
          result := 'Vortex Shaker';
        "X-ray Photoelectron Spectroscopy (XPS)":
          result := 'X-ray Photoelectron Spectroscopy';
        "Water contact angle":
          result := 'Drop shape analysis';
        "He pycnometry":
          result := 'Helium pycnometry';
        "XRD - crystalline phase":
          result := 'X-ray diffraction';
        "Electrophoretic Light Scattering":
          result := 'Electrophoretic Light Scattering';
        "Volumetric Cell Measurement (VCM)":
          result := 'Volumetric Centrifugation Method';
        "Batch Dispersion Quality":
          result := 'Batch dispersion quality Assay';
        "Sears titration":
          result := 'Sears titration';
        "Differential Centrifugal Sedimentation (DCS)":
          result := 'Centrifugal Liquid Sedimentation';
        "Raman Spectroscopy":
          result := 'Raman Spectroscopy';
        "COMET":
          result := 'In Vivo Mammalian Alkaline COMET Assay';
        "ESR spectroscopy", "ROS/EPR with Tempone-h":
          begin
            /* Check for correct mapping!*/          ;
            result := 'Electron Paramagnetic Resonance'
          end;
        "WST-1":
          result := 'WST-1 Metabolic Cell Viability Assay';
        "WST8":
          result := 'WST-8 Metabolic Cell Viability Assay';
        "ALAMAR BLUE":
          result := 'Alamar Blue Metabolic Cell Viability Assay';
        "ELISA", "ELISA MULTIPLEX":
          result := 'Enzyme-Linked Immunosorbent Assay';
        "Resazurin":
          result := 'Resazurin Metabolic Cell Viability Assay';
        "Fibroblast proliferation":
          begin
            /* Check for correct mapping! */          ;
            result := 'Cell Profiliration Assay'
          end;
        "Embryonic Stem Cell Test":
          result := 'Embryonic Stem Cell Test';
        "DCFH":
          result := 'Dichlorodihydrofluorescin diacetate';
        "DAN fluorimetric assay":
```

```
      result := 'DAN fluorimetric Assay';
    "Cytokinesis Block Micronucleus Cytome (CBMN Cyt)":
      result := 'Cytokinesis Block Micronucleus Cytome Assay';
    "MTT ASSAY":
      result := 'MTT Cell Viability Assay';
    "MTS CELL VIABILITY ASSAY":
      result := 'MTS Cell Viability Assay';
    "GSH":
      result := 'Glutathione Assay';
    "Haemolysis assay":
      result := 'Haemolysis Assay';
    "EPR analysis":
      result := 'Electron Paramagnetic Resonance';
    "Calcein-Ethidium":
      result := 'Calcein-Ethidium Assay';
    "CTA":
      result := 'Cell Transformation Assay';
    "CBMN assay":
      result := 'Cytokinesis Block Micronucleus Cytome Assay';
    "Griess Reagent", "Greiss Reagent":
      result := 'Griess Reagent Assay';
    "LUCIFER YELLOW":
      result := 'Lucifer Yellow Assay';
    "RT-PCR":
      result := 'Reverse transcription polymerase chain reaction';
    "Impedance flow cytometry":
      result := 'Impedance Flow Cytometry';
    "FRAS":
      result := 'Ferric Reduction Ability of Serum';
    "DCFH2-DA":
      result := 'Dichlorodihydrofluorescin diacetate';
    "Continuous Flow System (CFS)":
      result := 'Continuous Flow System';
    "STIS":
      result := 'Short Term Inhalation Study';
    "NR8383 alveolar macrophage assay":
      result := 'In vitro alveolar macrophage Assay';
    "Confocal microscopy":
      result := 'Confocal Optical Microscopy';
    "Electron Paramagnetic Resonance (EPR)":
      result := 'Electron Paramagnetic Resonance';
    "ZETA POTENTIAL":
      result := 'Electrophoretic Light Scattering';
    "OECD screening LoD or value, metal ion":
      result := 'Screening transformation/dissolution test - sparingly soluble metal compounds';
    "Oxiblot® kit (Millipore)":
      result := 'Protein Carbonylation Assay';
    "OECD TG 201", "OECD 201":
      result := 'Freshwater Alga and Cyanobacteria, Growth Inhibition Test';
    "OECD TG 202", "OECD 202":
      result := 'Daphnia sp. Acute Immobilisation Test';
    "NRF2ACTIVATION":
      result := 'NRF2 Activation Assay';
    "sequential GIT":
      result := 'Consecutive in vitro digestion Assay';
    "CFDA-AM":
      result := 'CFDA-AM Assay';
    "Impedance adherent cells":
      result := 'Impedance Analysis of Adherent Cells';
    "Isothermal Titration Calorimetry (ITC)":
      result := 'Isothermal Titration Calorimetry Assay';
    "Nanoparticle Tracking Analysis":
      result := 'Nanoparticle Tracking Analysis';
    "LUMINEX":
      result := 'LUMINEX Assay';
    "May grunwald giemsa coloration of BAL cells cytospin":
      result := 'May-Grunwald Giemsa coloration of BAL cells cytospin';
    "CFDA-AM":
      result := 'CFDA-AM Assay';
    "Pulse":
      result := 'Tunable Resistive Pulse Sensing'
    else
      result := 'Map article onto AssayDescriptor'('E.method_s')
  end
end
```

```
function EN_Study.'Map guidance_s onto AssayDescriptor'(p : EN_Params ): AssayDescriptor
  begin
    /* Tries to map an eNanoMapper study field E.guidance_s onto a GRACIOUS assay descriptor */  ;
    with 'Map abbreviation onto AssayDescriptor'(guidance_s) | assay_descriptor then
      result := assay_descriptor
    else
      case guidance_s of
        "CHN-ANALYSIS":
          result := 'CHN-Analysis';
        "dustiness-small drum":
          result := 'Small rotating Drum';
        "DUSTINESS WITH VORTEX SHAKER":
          result := 'Vortex Shaker';
        "RAMAN SPECTROSCOPY":
          result := 'Raman Spectroscopy';
        "ACELLULAR ESR FOR OXIDANT GENERATING POTENTIAL":
          begin
            /* To be checked.. */          ;
            result := 'Electron Paramagnetic Resonance'
          end;
        "BATCH DISPERSION QUALITY":
          result := 'Batch dispersion quality Assay';
        "EPR ANALYSIS", "ELECTRON PARAMAGNETIC RESONANCE (EPR)":
          result := 'Electron Paramagnetic Resonance';
        "DAN FLUORIMETRIC ASSAY":
          result := 'DAN fluorimetric Assay';
        "CBMN CYT":
          result := 'Cytokinesis Block Micronucleus Cytome Assay';
        "MTT":
          result := 'MTT Cell Viability Assay';
        "MTS":
          result := 'MTS Cell Viability Assay';
        "GSH":
          result := 'Glutathione Assay';
        "HAEMOLYSIS ASSAY":
          result := 'Haemolysis Assay';
        "CALCEIN-ETHIDIUM":
          result := 'Calcein-Ethidium Assay';
        "CELL TRANSFORMATION ASSAY (CTA)":
          result := 'Cell Transformation Assay';
        "MICRONUCLEUS":
          result := 'Cytokinesis Block Micronucleus Cytome Assay';
        "NO PRODUCTION":
          result := 'Griess Reagent Assay';
        "SCANNING ELECTRON MICROSCOPE (SEM)":
          result := 'Scanning Electron Microscopy';
        "SP_ICP-MS":
          result := 'Single Particle Inductively Coupled Plasma Mass Spectrometry';
        "FILTRATION ICP-MS":
          result := 'Filtration ICP-MS';
        "POTENTIOMETRY":
          result := 'Potentiometry Assay';
        "RT-PCR":
          result := 'Reverse transcription polymerase chain reaction';
        "IMPEDANCE FLOW CYTOMETRY":
          result := 'Impedance Flow Cytometry';
        "FERRIC REDUCTION ABILITY OF SERUM (FRAS)":
          result := 'Ferric Reduction Ability of Serum';
        "SHORT-TERM INHALATION STUDY PROTOCOL (STIS)":
          result := 'Short Term Inhalation Study';
        "IN VITRO ALVEOLAR MACROPHAGE ASSAY":
          result := 'In vitro alveolar macrophage Assay';
        "NPS INTRACELLULAR PENETRATION CONFOCAL MICROSCOPY":
          result := 'Confocal Optical Microscopy';
        "ZETA POTENTIAL":
          result := 'Electrophoretic Light Scattering';
        "OECD SCREENING LOD OR VALUE, METAL ION":
          result := 'Screening transformation/dissolution test - sparingly soluble metal compounds';
        "DETERMINING PROTEIN CARBONYLATION":
          result := 'Protein Carbonylation Assay';
        "H2DCFDA-PROBE":
          result := 'Dichlorodihydrofluorescin diacetate';
        "OECD TG408":
          begin
            /* Temporary check to avoid conflicting descriptor for COMET with wrong OECD TG 408 assigned to it.. */          ;
            if 'E.method_s' ≠ "COMET" then
```

```
            begin
              result := 'Repeated Dose 90-Day Oral Toxicity Study in Rodents'
            end
          end;
        "IMPEDANCE ADHERENT CELLS":
          result := 'Impedance Analysis of Adherent Cells';
        "ISOTHERMAL TITRATION CALORIMETRY (ITC)":
          result := 'Isothermal Titration Calorimetry Assay';
        "NANOPARTICLE SIZE ANALYZER":
          result := 'Nanoparticle Tracking Analysis';
        "RESAZURIN":
          result := 'Resazurin Metabolic Cell Viability Assay'
        else
          result := 'Map article onto AssayDescriptor'(guidance_s)
      end
  end

function EN_Study::'Map ontology entry onto AssayDescriptor'(str : String,p : EN_Params ):: AssayDescriptor
  case str of
    "NPO_1430":
      result := 'Transmission Electron Microscopy';
    "ENM_8000310", "CHMO_0000207":
      result := 'Wide-Angle X-ray Scattering';
    "OBI_0002108", "CHMO_0000204":
      result := 'Small Angle X-ray Scattering';
    "NPO_1469":
      result := 'Dynamic Light Scattering';
    "NPO_1709":
      result := 'Lactate DeHydrogenase Assay';
    "OBI_0302736":
      result := 'In Vivo Mammalian Alkaline COMET Assay';
    "NPO_1340":
      /* refers to cytotoxicity in general, not specific enough to distinghish between differen cytotoxicity assays */    ;
    "ENM_9000013":
      /* wst-1 cell proliferation assay is a sensitive and accurate assay for cell proliferation and cytotoxicity. */    ;
    "ENM_8000277":
      result := 'Neutral Red Uptake Cell Viability Assay';
    "CHMO_0002123":
      result := 'Electrophoretic Light Scattering'
  end
```

```
function EN_Study::'Map abbreviation onto AssayDescriptor'(str : String ):: AssayDescriptor
  begin
    /* Tries to map an eNanoMapper study field string value as potential method abbreviation onto a GRACIOUS assay descriptor */  ;
    case str of
      "ELS":
        result := 'Electrophoretic Light Scattering';
      "EDX":
        result := 'Energy-Dispersive X-ray Spectroscopy';
      "TEM":
        result := 'Transmission Electron Microscopy';
      "SEM":
        result := 'Scanning Electron Microscopy';
      "ICP-MS":
        result := 'Inductively Coupled Plasma Mass Spectrometry';
      "XRF":
        result := 'X-Ray Fluorescence';
      "TG", "TGA":
        result := 'Thermogravimetry';
      "TGA-MS":
        result := 'Thermogravimetric Analysis/Mass Spectrometry';
      "ES-DMA":
        result := 'ElectroSpray-Differential Mobility Analysis';
      "CLS", "DCS":
        result := 'Centrifugal Liquid Sedimentation';
      "ICP-OES":
        result := 'Inductively Coupled Plasma Optical Emission Spectrometry';
      "WAXS":
        result := 'Wide-Angle X-ray Scattering';
      "SAXS":
        result := 'Small Angle X-ray Scattering';
      "DLS":
        result := 'Dynamic Light Scattering';
      "LDH":
        result := 'Lactate DeHydrogenase Assay';
      "XPS":
        result := 'X-ray Photoelectron Spectroscopy';
      "DSA":
        result := 'Drop shape analysis';
      "BET":
        result := 'Brunauer-Emmett-Teller method';
      "XRD":
        result := 'X-ray diffraction';
      "AU", "AUC":
        result := 'Analytical Ultracentrifugation';
      "VCM":
        result := 'Volumetric Centrifugation Method';
      "NRU":
        result := 'Neutral Red Uptake Cell Viability Assay';
      "CFE":
        result := 'Colony Forming Efficiency Assay';
      "TEER":
        result := 'TransEpithelial Electrical Resistance Assay';
      "ELISA":
        result := 'Enzyme-Linked Immunosorbent Assay';
      "DCFH":
        result := 'Dichlorodihydrofluorescin diacetate';
      "MDA":
        result := 'Lipid Peroxidation (MDA) Assay';
      "EPR":
        result := 'Electron Paramagnetic Resonance';
      "FRAS":
        result := 'Ferric Reduction Ability of Serum';
      "DCFH2-DA":
        result := 'Dichlorodihydrofluorescin diacetate';
      "CFS":
        result := 'Continuous Flow System';
      "STIS":
        result := 'Short Term Inhalation Study';
      "EPR":
        result := 'Electron Paramagnetic Resonance';
      "NTA":
        result := 'Nanoparticle Tracking Analysis'
    end
  end
```

```
function EN_Study::'Map article onto AssayDescriptor'(str : String ):: AssayDescriptor
  begin
    /* Peer review needed! */  ;
    case str of
      "HTTPS://DOI.ORG/10.1021/AC60120A048":
        result := 'Sears titration'
    end
  end
```

Class `EN_StudyResult` is kind of `EN_Study`

Attributes

name	type	domain	inference	comment
id	: String			
name_s	: String			
publicname_s	: String			
owner_name_s	: String			
substanceType_s	: String			
type_s	: String			
investigation_uuid_s	: String			
assay_uuid_s	: String			
endpointcategory_s	: String			
endpoint_s	: String			
effectendpoint_s	: String			
effectendpoint_type_s	: String			
effectendpoint_synonym_ss	: Strings			
reference_owner_s	: String			
reference_year_s	: String			
reference_s	: String			
textValue_s	: String			
interpretation_result_s	: String			
loValue_d	: Real			
upValue_d	: Real			
err_d	: Real			
errQualifier_s	: String			
unit_s	: String			
updated_s	: String			
studyResultType_s	: String			
version	: Integer			
'E.cell_type_s'	: String			

Operators

```
function EN_StudyResult.DirectlyProvided(): Boolean [specialization]
  begin
    /* The study doesn't contain results from a specific assay, but the result are directly provided. */  ;
    if ('E.method_s' = "") or ('E.method_s' = "supplier") then
    begin
      case guidance_s of
        "NANOREG SUPPLIER":
          result := True;
        "":
          begin
            if endpointcategory_s = "GI_GENERAL_INFORM_SECTION" then
              result := True
          end
      end
    end
  end


function EN_StudyResult.MapTo_CategoryEndpointDescriptor(): any Enumeration
  case topcategory_s of
    "P-CHEM":
      result := MapTo_PC_CategoryEndpointDescriptor();
    "TOX":
      result := MapTo_HH_CategoryEndpointDescriptor();
    "ECOTOX":
      result := MapTo_EC_CategoryEndpointDescriptor()
  end
```

```
function EN_StudyResult.MapTo_PC_CategoryEndpointDescriptor(): any Enumeration
  case endpointcategory_s of
    "CRYSTALLINE_PHASE_SECTION":
      result := PC_CRYSTALLINE_PHASE;
    "SURFACE_CHEMISTRY_SECTION":
      result := PC_SURFACE_CHEMISTRY;
    "PC_GRANULOMETRY_SECTION":
      result := PC_GRANULOMETRY;
    "SPECIFIC_SURFACE_AREA_SECTION":
      result := PC_SPECIFIC_SURFACE_AREA;
    "ASPECT_RATIO_SHAPE_SECTION":
      result := PC_ASPECT_RATIO_SHAPE;
    "ENM_0000081_SECTION":
      begin
        /*batch dispersion, mapped onto granulometry for now??*/      ;
        result := PC_GRANULOMETRY
      end;
    "DUSTINESS_SECTION":
      result := PC_DUSTINESS;
    "ANALYTICAL_METHODS_SECTION":
      begin
        /* ?? */      ;
        result := PC_COMPOSITION
      end;
    "ZETA_POTENTIAL_SECTION":
      result := PC_ZETA_POTENTIAL;
    "PC_WATER_SOL_SECTION":
      result := PC_WATER_SOL;
    "ENM_8000223_SECTION":
      begin
        /* Aerosol Characterisation Assay, THIS IS NOT AN Category Endpoint!! */      ;
        result := PC_AEROSOL_CHARACTERISATION
      end;
    "CRYSTALLITE_AND_GRAIN_SIZE_SECTION":
      result := PC_CRYSTALLITE_AND_GRAIN_SIZE;
    "POROSITY_SECTION":
      result := PC_POROSITY;
    "PC_DENSITY_SECTION":
      result := PC_DENSITY;
    "PC_SOL_ORGANIC_SECTION":
      result := PC_SOL_ORGANIC;
    "GI_GENERAL_INFORM_SECTION":
      begin
        /* Mapped onto PC_APPEARANCE */      ;
        result := PC_APPEARANCE
      end;
    "IMPURITY_SECTION":
      result := PC_COMPOSITION;
    "SURFACE_TENSION_SECTION":
      result := PC_SURFACE_TENSION;
    "PC_THERMAL_STABILITY_SECTION":
      result := PC_STABILITY_THERMAL_SUNLIGHT_METALS;
    "AGGLOMERATION_AGGREGATION_SECTION":
      result := PC_AGGLOMERATION_AGGREGATION;
    "RADICAL_FORMATION_POTENTIAL_SECTION":
      result := PC_RADICAL_FORMATION_POTENTIAL;
    "BIO_NANO_INTERACTION_SECTION":
      result := PC_BIOMOL_INTERACTION
  end


function EN_StudyResult.MapTo_EN_CategoryEndpointDescriptor(): any Enumeration
  case endpointcategory_s of
    "ENM_0000081_SECTION":
      begin
        /*batch dispersion mapped onto granulometry for now??*/      ;
        result := PC_GRANULOMETRY
      end;
    "ANALYTICAL_METHODS_SECTION":
      begin
        /*??*/      ;
        result := nil
      end
  end
```

```
function EN_StudyResult.MapTo_EC_CategoryEndpointDescriptor(): any Enumeration
  case endpointcategory_s of
    "EC_DAPHNIATOX_SECTION":
      begin
        /* This is covered by EC_AQUATIC_INVERT_TOX_SHORT, EC_AQUATIC_INVERT_TOX_CHRONIC */      ;
        result := EC_AQUATIC_INVERT_TOX_SHORT
      end;
    "EC_SOILDWELLINGTOX_SECTION":
      result := nil;
    "EC_FISHTOX_SECTION":
      begin
        /* Not sure which section to map to short or chronic */      ;
        result := EC_FISH_TOX_SHORT
      end;
    "EC_SOIL_MICRO_TOX_SECTION":
      result := EC_SOIL_MICRO_TOX;
    "UNKNOWN_TOXICITY_SECTION":
      result := nil;
    "EC_PLANTTOX_SECTION":
      result := EC_TERR_PLANT_TOX;
    "EC_ALGAETOX_SECTION":
      result := EC_ALGAE_TOX
  end

function EN_StudyResult.MapTo_HH_CategoryEndpointDescriptor(): any Enumeration
  case endpointcategory_s of
    "ENM_0000068_SECTION":
      begin
        /* viability */      ;
        result := HH_CYTOTOXICITY
      end;
    "ENM_0000037_SECTION":
      begin
        /* oxidative stress */      ;
        result := HH_OXIDATIVE_STRESS
      end;
    "NPO_1339_SECTION":
      begin
        /* immunotoxicity */      ;
        result := HH_IMMUNOTOXICITY
      end;
    "TO_GENETIC_IN_VITRO_SECTION":
      result := HH_GENETIC_IN_VITRO;
    "TO_ACUTE_INHAL_SECTION":
      result := HH_ACUTE_TOX_INHAL;
    "TO_REPEATED_INHAL_SECTION":
      result := HH_REPEATED_INHAL;
    "ENM_0000044_SECTION":
      begin
        /* barrier integrity */      ;
        result := HH_BARRIER_INTEGRITY
      end;
    "TO_REPEATED_ORAL_SECTION":
      begin
        result := HH_REPEATED_ORAL
      end;
    "TO_GENETIC_IN_VIVO_SECTION":
      result := HH_GENETIC_IN_VIVO;
    "UNKNOWN_TOXICITY_SECTION":
      result := nil
  end
```

```
function EN_StudyResult.MapTo_ResultEndpointDescriptors( assay_descriptor :: AssayDescriptor ): Enumerates
  with MapTo_CategoryEndpointDescriptor() | category_endpoint then
  begin
    with category_endpoint→Enumerates | eps then
    begin
      with eps→Any(ep | ep→Name in effectendpoint_synonym_ss) | syn_map then
        /* result→Add(syn_map)*/
    end;
    with 'Map abbreviation onto result endpoint descriptor'(endpoint_s) | abbr_map then
    begin
      result→Add(abbr_map)
    end;
    with 'Map abbreviation onto result endpoint descriptor'(effectendpoint_s) | abbr_map then
    begin
      result→Add(abbr_map)
    end;
    with 'Map endpoint_s onto ResultEndpointDescriptor'(category_endpoint) | endpoint_s_map then
    begin
      result→Add(endpoint_s_map)
    end;
    with 'Map effectendpoint_s onto result endpoint descriptor'(category_endpoint, assay_descriptor) | endpoint_s_map then
    begin
      result→Add(endpoint_s_map)
    end;
    foreach syn of effectendpoint_synonym_ss do
    begin
      with 'Map ontology entry onto result endpoint descriptor'(category_endpoint, syn) | onto_map then
        result→Add(onto_map)
    end;
    result := result→Select(ep | ep ≠ nil)→Unique
  end

function EN_StudyResult::'Map abbreviation onto result endpoint descriptor'( str : String ):: any Enumerate
  case str of
    "SBET", "MSSA":
      result := PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA;
    "VSSA":
      result := PC_SPECIFIC_SURFACE_AREA::EP_VOLUME_SPECIFIC_SURFACE_AREA;
    "IEP", "pI", "pH(I)":
      result := PC_ZETA_POTENTIAL::EP_ISOELECTRIC_POINT
  end
```

```
function EN_StudyResult.'Map endpoint_s onto ResultEndpointDescriptor'(category_endpoint :: any Enumeration ): any Enumerate
  case category_endpoint of
    PC_SURFACE_CHEMISTRY:
      begin
        case endpoint_s of
          "SURFACE CHEMISTRY":
            begin
              /*result := PC_COMPOSITION::EP_ELEMENT_RECORD*/            ;
              result := PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC
              end
              end
              end;
              PC_COMPOSITION:
              begin
                case endpoint_s of
                  "ELEMENTAL COMPOSITION AND CHEMICAL PURITY":
                    begin
                      /*result := PC_COMPOSITION::EP_ELEMENT_RECORD*/                    ;
                      result := EP_ELEMENTAL_COMPOSITION_MASS_CONC
                      end
                      end
                      end;
                      PC_CRYSTALLINE_PHASE:
                      begin
                        case endpoint_s of
                          "CRYSTALLINE PHASE":
                            result := PC_CRYSTALLINE_PHASE::EP_SPACE_GROUP;
                          "POLYMORPHISM":
                            begin
                              result := PC_CRYSTALLINE_PHASE::EP_MINERAL_NAME
                              end
                              end
                              end;
                              PC_SURFACE_TENSION:
                              begin
                                case endpoint_s of
                                  "WATER CONTACT ANGLE", "HYDROPHOBICITY (WATER CONTACT ANGLE)":
                                    result := PC_SURFACE_TENSION::EP_WATER_CONTACT_ANGLE
                          end
                          end;
                          PC_WATER_SOL:
                          begin
                            case endpoint_s of
                            "DISSOLUTION HALFTIME AND RATE", "DISSOLUTION RATE IN RELEVANT HUMAN MEDIUM (LYSOSOMAL DISSOLUTION RATE K)":
                            begin
                              case effectendpoint_s of
                              "ELEMENT DETECTED":
                              /* not sure what this is about */                                    ;
                              "HALF TIME":
                              result := PC_WATER_SOL::EP_DISSOLUTION_HALF_TIME;
                              "DISSOLUTION RATE":
                              result := PC_WATER_SOL::EP_DISSOLUTION_RATE
                            end
                          end;
                          "SOLUBILITY IN WATER (OECD SCREENING LOD OR VALUE, METAL ION)":
                          begin
                            case effectendpoint_s of
                            "SOLUBILITY":
                            result := PC_WATER_SOL::EP_SOLUBILITY
                            else
                            result := PC_WATER_SOL::EP_SOLUBILITY
                          end
                        end
      end
    end
end;
HH_CYTOTOXICITY:
begin
  case endpoint_s of
  "CELL GROWTH & CYTOTOXICITY : WST-1 ASSAY", "CELL_VIABILITY":
  begin
    /* SEE ALSO MAPPING OF EFFECTENPOINT_S=> CELL VIABILITY */                          ;
    result := HH_CYTOTOXICITY::EP_CELL_VIABILITY
  end;
  "CULTURE AND EXPOSURE OF MOUSE PRIMARY LUNG FIBROBLASTS", "PROTOCOL CULTURE AND EXPOSURE OF MOUSE PRIMARY LUNG FIBROBLASTS":
  begin
```

```
                /* Check for correct mapping! DEVIATES from CATEGORY */                          ;
                result := HH_FIBROSIS::EP_FIBROSIS
              end
            end
          end;
          HH_FIBROSIS:
          begin
            case endpoint_s of
            "CULTURE AND EXPOSURE OF MOUSE PRIMARY LUNG FIBROBLASTS", "PROTOCOL CULTURE AND EXPOSURE OF MOUSE PRIMARY LUNG FIBROBLASTS":
            begin
              /* Check for correct mapping! */                          ;
              result := HH_FIBROSIS::EP_FIBROSIS
            end
          end
        end;
      PC_RADICAL_FORMATION_POTENTIAL:
        begin
          case endpoint_s of
          "OXIDATIVE STRESS", "AIR LIQUID INTERFACE":
          begin
            case effectendpoint_s of
            "PERCENTAGE_OF_CONTROL":
            result := EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL
          end
        end
    end
  end;
  EC_ALGAE_TOX:
  begin
    case endpoint_s of
    "GROWTH INHIBITION":
    begin
      /* Check if growth inhibition is the same as growth endpoint */                ;
      result := EC_ALGAE_TOX::EP_GROWTH
    end
  end
end;
        EC_AQUATIC_INVERT_TOX_SHORT:
          begin
            case endpoint_s of
            "IMMOBILISATION", "IMMOBILISATION ":
            result := EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION
          end
      end;
      EC_FISH_TOX_SHORT:
      begin
        case endpoint_s of
        "LYSOSOMAL INTEGRITY":
        result := EC_FISH_TOX_SHORT::EP_LYSOSOMAL_INTEGRITY;
        "METABOLIC ACTIVITY":
        result := EC_FISH_TOX_SHORT::EP_METABOLIC_ACTIVITY;
        "PLASMA MEMBRANE INTEGRITY":
        result := EC_FISH_TOX_SHORT::EP_PLASMA_MEMBRANE_INTEGRITY
      end
    end
  end
```

```
function EN_StudyResult.'Map effectendpoint_s onto result endpoint descriptor'(category_endpoint :: any Enumeration,assay_descriptor :: AssayDescriptor ): any Enumerate
  case category_endpoint of
    PC_APPEARANCE:
      begin
        case effectendpoint_s of
          "PHYSICAL_STATE":
            result := PC_APPEARANCE::EP_PHYSICAL_STATE
        end
          end;
        PC_COMPOSITION:
          begin
            begin
              case effectendpoint_s of
                "CONTRIBUTION":
                  begin
                    case unit_s of
                      "at%":
                        result := EP_ELEMENTAL_COMPOSITION_ATOM_PERC
                      else
                      result := EP_ELEMENTAL_COMPOSITION_MASS_CONC
                        end
                      end
                        end
                      end
                        end;
                      PC_WATER_SOL:
                        begin
                          case effectendpoint_s of
                            "% DISSOLVED":
                              result := PC_WATER_SOL::EP_PERCENTAGE_DISSOLVED
                          end
                            end;
                          PC_SURFACE_CHEMISTRY:
                            begin
                              case endpoint_s of
                                "SURFACE CHEMISTRY":
                                  begin
result := PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_ATOM_PERC
end;
"CHEMICAL COMPOSITION OF PARTICLES":
begin
  case effectendpoint_s of
    "PURITY OF PARTICLES":
      result := PC_COMPOSITION::EP_PURITY;
    "INORGANIC COAT./ASS. ELEMENTS":
      result := PC_SURFACE_CHEMISTRY::EP_NOMINAL_INORGANIC_COMPOSITION;
    "ORGANIC COAT./ASS. ORGANICS":
      result := PC_SURFACE_CHEMISTRY::EP_NOMINAL_ORGANIC_COMPOSITION
    end
      end;
    "COATING":
      begin
        case effectendpoint_s of
          "CONTRIBUTION":
            begin
              case unit_s of
                "%w/w":
                  result := PC_COMPOSITION::EP_ELEMENTAL_COMPOSITION_MASS_CONC
                end
                  end
                end
                  end
                end
                  end;
                PC_DENSITY:
                  begin
                    case effectendpoint_s of
                      "DENSITY_SKELETAL":
                        result := PC_DENSITY::EP_SKELETAL_DENSITY
                      end
                        end;
                      PC_GRANULOMETRY:
                        begin
                          case endpoint_s of
                            "NOMINAL DIAMETER & LENGTH":
```

```
  case effectendpoint_s of
    "DIAMETER":
      result := PC_GRANULOMETRY::EP_NOMINAL_DIAMETER;
    "LENGTH":
      result := PC_GRANULOMETRY::EP_NOMINAL_LENGTH
  end;
"DISPERSION QUALITY":
  begin
    case effectendpoint_s of
      "HYDRODYNAMIC DIAMETER":
        begin
          if effectendpoint_type_s = "Z_AVERAGE" then
            result := PC_GRANULOMETRY::EP_Z_AVERAGE_DIAMETER
          end;
          "BATCH DISPERSION SIZE DISTRIBUTION":
          result := PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER
          end
          end;
          "SIZE", "PARTICLE SIZE DISTRIBUTION (GRANULOMETRY)":
          begin
            case effectendpoint_s of
              "HYDRODYNAMIC DIAMETER":
                case effectendpoint_type_s of
                  "Z-AVERAGE":
                    result := PC_GRANULOMETRY::EP_Z_AVERAGE_DIAMETER
                end;
              "VOLUME DIAMETER":
                begin
                  /* Not clear what this is about.*/                                                                    ;
                  result := PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER
                  end;
                  "DERIVED COUNT RATE":
                  begin
                    result := PC_GRANULOMETRY::EP_DERIVED_COUNT_RATE
                    end;
                    "GLOBAL MEAN SIZE":
                    case effectendpoint_type_s of
  "INTENSITY-WEIGHTED":
    result := PC_GRANULOMETRY::EP_INTENSITY_WEIGHTED_SIZE
end;
"SIZE (MASS)":
begin
  case effectendpoint_type_s of
    "D50":
      /*result := PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE EP_DmPx_D1, AUC measures equivalent settling sphere..*/
                                                                                                                      ;
    "D_MAX":
      /* result := PC_GRANULOMETRY::EP_DmPx_
         D3*/                                                                                                  end
      end;
    "SIZE (DISTRIBUTION)":
      begin
        case effectendpoint_type_s of
          "D10", "D50", "D90":
            begin
              /* AUC measures equivalent settling sphere..*/
                                                                                                                  ;
              result := PC_GRANULOMETRY::EP_DnPx_D1
              end
              end
              end;
              "HALF_HEIGHT_PEAK_WIDTH":
              begin
                result := EP_FULL_WIDTH_AT_HALF_MAXIMUM
                end
                end
                end;
                "SIZE DISTRIBUTION":
                begin
                  case effectendpoint_s of
                    "HYDRODYNAMIC DIAMETER":
                      result := PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER
                    end
                      end;
                    "ES-DMA":
                      begin
```

```
      case effectendpoint_s of
        "DIAMETER (NUMBER)":
          result := PC_GRANULOMETRY::EP_ELECTRICAL_MOBILITY_EQ_SPHERE_DIAMETER;
        "HALF_HEIGHT_PEAK_WIDTH":
          result := EP_FULL_WIDTH_AT_HALF_MAXIMUM
        end
          end;
        "TEM":
          begin
            case effectendpoint_s of
              "FERET MINIMAL DIAMETER":
                result := EP_FERET_DIAMETER_D1
            end
          end
      end;
      case effectendpoint_s of
      "SIZE DISTRIBUTION":
      begin
        if assay_descriptor = 'Nanoparticle Tracking Analysis' then
          result := PC_GRANULOMETRY::EP_HYDRODYNAMIC_EQ_SPHERE_DIAMETER
      end;
      "ECD":
      result := PC_GRANULOMETRY::EP_EQUIVALENT_CIRCLE_DIAMETER;
      "LENGTH":
      result := PC_GRANULOMETRY::EP_FERET_DIAMETER_D3;
      "PRIMARY_PARTICLE_SIZE":
      begin
        case effectendpoint_type_s of
        "MIN":
        result := PC_GRANULOMETRY::EP_PRIMARY_PARTICLE_DIAMETER;
        "MAX":
        result := PC_GRANULOMETRY::EP_PRIMARY_PARTICLE_LENGTH
      end
    end;
  "PDI":
    result := PC_GRANULOMETRY::EP_DISPERSITY
end
                end;
                PC_SPECIFIC_SURFACE_AREA:
                begin
                  case endpoint_s of
                  "SSA", "SURFACE AREA":
                  case effectendpoint_s of
                  "VSSA":
                  result := PC_SPECIFIC_SURFACE_AREA::EP_VOLUME_SPECIFIC_SURFACE_AREA;
                  "SBET", "MSSA":
                  result := PC_SPECIFIC_SURFACE_AREA::EP_MASS_SPECIFIC_SURFACE_AREA;
                  "EXTERNAL SURFACE ST":
                  result := PC_SPECIFIC_SURFACE_AREA::EP_MASS_EXTERNAL_SURFACE;
                  "MICROPOROSITY SURFACE SU":
                  result := PC_SPECIFIC_SURFACE_AREA::EP_MASS_MICROPOROSITY_SURFACE
                end
              end
            end;
          PC_ASPECT_RATIO_SHAPE:
            begin
              case endpoint_s of
              "SIZE SHAPE":
              begin
                case effectendpoint_s of
                "CIRCULARITY":
                result := PC_ASPECT_RATIO_SHAPE::EP_CIRCULARITY;
                "ROUNDNESS":
                result := PC_ASPECT_RATIO_SHAPE::EP_ROUNDNESS;
                "SOLIDITY":
                result := PC_ASPECT_RATIO_SHAPE::EP_SOLIDITY
              end
            end
        end;
        case effectendpoint_s of
        "ASPECT_RATIO_D3_D1":
        result := PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1
      end
end;
PC_AEROSOL_CHARACTERISATION:
begin
```

```
            case endpoint_s of
            "AEROSOL CHARACTERISATION":
            if effectendpoint_s = "NUMBER OF PARTICLES/CM3" then
              result := PC_AEROSOL_CHARACTERISATION::EP_AEROSOLISED_PARTICLE_CONC
          end
        end;
        PC_POROSITY:
        begin
          case effectendpoint_s of
          "PORE_RADIUS":
          result := PC_POROSITY::EP_PORE_RADIUS
        end
      end;
      PC_SURFACE_TENSION:
      begin
        case endpoint_s of
        "CONTACT ANGLE 0":
        result := PC_SURFACE_TENSION::EP_WATER_CONTACT_ANGLE
      end
    end;
  PC_ZETA_POTENTIAL:
    begin
      begin
        case effectendpoint_s of
        "ZETA POTENTIAL":
        result := PC_ZETA_POTENTIAL::EP_ZETA_POTENTIAL
      end
    end
end;
PC_STABILITY_THERMAL_SUNLIGHT_METALS:
begin
  case effectendpoint_s of
  "WEIGHT LOSS (ORGANICS)":
  result := PC_STABILITY_THERMAL_SUNLIGHT_METALS::EP_MASS_LOSS;
  "WEIGHT LOSS (WATER)":
  result := PC_STABILITY_THERMAL_SUNLIGHT_METALS::EP_MASS_LOSS_WATER
end
  end;
  PC_RADICAL_FORMATION_POTENTIAL:
  begin
    case effectendpoint_s of
    "AUC":
    begin
      case effectendpoint_type_s of
      "MASS":
      result := PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_MASS;
      "SURFACE":
      result := PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_AUC_SURFACE
    end
  end;
  "OXIDATIVE_DAMAGE":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_OXIDATIVE_DAMAGE_PER_DOSE
  end;
  "FRAS_SCORE_MASS":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_FRAS_SCORE_MASS
  end;
  "FRAS_SCORE_SURFACE", "FRASS_SCORE_SURFACE":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_FRAS_SCORE_SURF
  end;
  "SPIN_COUNT":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_SPIN_COUNT_PER_SURFACE_CONC
  end;
  "SURFACE REACTIVITY (CPH/DH2O)":
  begin
    case effectendpoint_type_s of
    "MASS":
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_MASS;
    "SURFACE":
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_CPH_DH20_SURF
  end
end;
```

```
    "SURFACE REACTIVITY (DMPO/DH2O)":
      begin
        case effectendpoint_type_s of
        "MASS":
        result := PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_MASS;
        "SURFACE":
        result := PC_RADICAL_FORMATION_POTENTIAL::EP_SURFACE_REACTIVITY_DMPO_DH20_SURF
      end
  end;
  "ROS GENERATION":
  begin
    /* DCFH2-DA */                                                                    ;
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_ROS_GENERATION_AU
  end;
  "FLUORESCENCE 480/530":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_FLUORESCENCE_480_530_AU
  end;
  "DCFH_OXIDATION":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_OXIDATION_MASS
  end;
  "DCFH_SCORE":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_SCORE_MASS
  end;
  "EPR_SCORE_SURFACE":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_SURF
  end;
  "EPR_SCORE_MASS":
  begin
    result := PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SCORE_MASS
  end;
  "EPR_SIGNAL_INTENSITY":
  begin
    case effectendpoint_type_s of
                  "PERCENTAGE_OF_CONTROL":
                  result := PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY_PERC_OF_CONTROL
                  else
                  result := PC_RADICAL_FORMATION_POTENTIAL::EP_EPR_SIGNAL_INTENSITY
                end
              end
          end
        end;
      PC_BIOMOL_INTERACTION:
        begin
          case effectendpoint_s of
          "BINDING ENERGY":
          result := PC_BIOMOL_INTERACTION::EP_BINDING_ENERGY;
          "BINDING ENTHALPY":
          result := PC_BIOMOL_INTERACTION::EP_BINDING_ENTHALPY;
          "BINDING ENTROPY":
          result := PC_BIOMOL_INTERACTION::EP_BINDING_ENTROPY
        end
    end;
    EC_AQUATIC_INVERT_TOX_SHORT:
    begin
      case endpoint_s of
      "FRESHWATER TOXICITY":
      begin
        /* According to OECD TG202 => Immobilization */                                ;
        result := EC_AQUATIC_INVERT_TOX_SHORT::EP_IMMOBILIZATION
      end
    end
  end;
HH_OXIDATIVE_STRESS:
  begin
    case endpoint_s of
    "AIR LIQUID INTERFACE":
    begin
      if effectendpoint_s = "PERCENTAGE_OF_CONTROL" then
        result := EP_DCFH_AIR_LIQUID_INTERFACE_PERC_OF_CONTROL
    end;
    "OXIDATIVE STRESS":
```

```
begin
  if effectendpoint_s = "PERCENTAGE_OF_CONTROL" then
    result := EP_DCFH_OXIDATIVE_STRESS_PERC_OF_CONTROL
end;
"CARBONYLATION, DOTBLOT":
begin
  if effectendpoint_s = "CARBONYLATION" then
    if effectendpoint_type_s = "IOD NORMALIZED FOR UG PROTEIN" then
      result := HH_OXIDATIVE_STRESS::EP_CARBONYLATION_IOD_NORMALIZED_FOR_UG_PROTEIN
end
else
case effectendpoint_s of
"INTRINSIC ROS CHANGE IN RFU":
begin
  /* Intrinsic DCFH2-DA is acellular therefore belong under section PC_RADICAL_FORMATION_
     POTENTIAL */                                                                    ;
  result := PC_RADICAL_FORMATION_POTENTIAL::EP_DCFH_INTRINSIC_ROS_CHANGE_IN_RFU
end;
"CHANGE RFU":
begin
  /* Check if this is actuall a cellular endpoint..  */                                ;
  result := HH_OXIDATIVE_STRESS::EP_DCFH_RFU_CHANGE
end;
"LUCIFERASE ACTIVITY":
begin
  result := HH_OXIDATIVE_STRESS::EP_NRF2_LUCIFERASE_ACTIVITY
end;
"FOLD LUCIFERASE ACTIVITY INDUCTION":
begin
  result := HH_OXIDATIVE_STRESS::EP_NRF2_FOLD_LUCIFERASE_ACTIVITY_INDUCTION
end;
"CHANGE IN GSH LEVEL":
begin
  result := HH_OXIDATIVE_STRESS::EP_CHANGE_IN_GSH_LEVEL
end;
"LIPID PEROXIDATION":
begin
          /*  */                                                                    ;
          result := HH_OXIDATIVE_STRESS::EP_MDA_LIPID_PEROXIDATION
        end
      end
    end
  end;
HH_CYTOTOXICITY:
  begin
    case endpoint_s of
    "CELL VIABILITY":
    case effectendpoint_s of
    "ABSORPTION AT 450 NM":
    result := EP_WST_CELL_VIABILITY_ABSORPTION_450_NM;
    "ABSORPTION AT 540 NM":
    result := HH_CYTOTOXICITY::EP_NRU_CELL_VIABILITY_ABSORPTION_540_NM
    else
    result := HH_CYTOTOXICITY::EP_CELL_VIABILITY
  end;
"VIABILITY", "AIR LIQUID INTERFACE", "CYTOTOXICITY", "CYTOTOX", "% CYTOTOXICITY", "% CELLULAR LDH/CONTROL", "% CELL VIABILITY":
  case effectendpoint_s of
"PERCENTAGE_OF_CONTROL":
  case assay_descriptor of
'Lactate DeHydrogenase Assay':
  result := HH_CYTOTOXICITY::EP_LDH_CYTOTOXICITY_PERC_OF_CONTROL;
'Alamar Blue Metabolic Cell Viability Assay':
  result := HH_CYTOTOXICITY::EP_ALAMAR_BLUE_CYTOTOXICITY_PERC_OF_CONTROL;
'MTS Cell Viability Assay':
  result := HH_CYTOTOXICITY::EP_MTS_CYTOTOXICITY_PERC_OF_CONTROL;
'Neutral Red Uptake Cell Viability Assay':
  result := HH_CYTOTOXICITY::EP_NRU_VIABILITY_PERC_OF_CONTROL;
'Resazurin Metabolic Cell Viability Assay':
  result := HH_CYTOTOXICITY::EP_RESAZURIN_VIABILITY_PERC_OF_CONTROL;
'Impedance Analysis of Adherent Cells':
  result := HH_CYTOTOXICITY::EP_IAAC_CYTOTOXICITY_PERC_OF_CONTROL;
'WST-1 Metabolic Cell Viability Assay':
  result := HH_CYTOTOXICITY::EP_WST_VIABILITY_PERC_OF_CONTROL;
'Colony Forming Efficiency Assay':
  result := HH_CYTOTOXICITY::EP_CFE_CYTOTOXICITY_PERC_OF_CONTROL
```

```
                    end;
                    "NORMALISED POST-EXPOSURE CELL INDEX 1":
                    begin
                      /* NanoReg Impedance Analysis of Adherent Cells */                                                    ;
                      result := HH_CYTOTOXICITY::EP_NORMALISED_POST_EXPOSURE_CELL_INDEX_1
                    end;
                    "ABSORBANCE AT 420-480 NM":
                    begin
                      result := HH_CYTOTOXICITY::EP_WST_CELL_VIABILITY_ABSORPTION_420_480_NM
                    end
                  end;
                "% DECREASE AT MAX DOSE":
                  result := HH_CYTOTOXICITY::EP_ALAMAR_BLUE_PERC_DECREASE_AT_MAX_DOSE
              end
            end;
            HH_IMMUNOTOXICITY:
            begin
              case endpoint_s of
              "AIR LIQUID INTERFACE", "IMMUNOTOXICITY":
              case effectendpoint_s of
              "IL-6 CONCENTRATION", "IL-10 CONCENTRATION", "IL-12 CONCENTRATION", "TNF-A CONCENTRATION":
              begin
                case assay_descriptor of
                'LUMINEX Assay':
                result := EP_LUMINEX_IN_VITRO_CYTOKINE_SECRETION;
                'Enzyme-Linked Immunosorbent Assay':
                begin
                  /* ELISA */                                                ;
                  result := HH_INFLAMMATION::EP_IN_VITRO_CYTOKINE_RELEASE
                end
              end
            end
          end
        end
      end;
    HH_GENETIC_IN_VITRO:
      begin
        case effectendpoint_s of
        "DNA STRAND BREAKS":
        result := HH_GENETIC_IN_VITRO::EP_DNA_STRAND_BREAKS;
        "NET FPG SITES":
        result := HH_GENETIC_IN_VITRO::EP_FPG_SENSITIVE_SITES
      end
    end;
    HH_ACUTE_TOX_INHAL:
    begin
      case endpoint_s of
      "SHORT-TERM INHALATION STUDY PROTOCOL (STIS)":
      case effectendpoint_s of
      "CATEGORY":
      result := EP_TOX_CATEGORY_STIS
    end
  end
end;
HH_REPEATED_ORAL:
begin
  case endpoint_s of
  "BALL ANALYSIS":
  case effectendpoint_s of
  "TOTAL NUMBER OF CELLS IN BAL":
  result := HH_REPEATED_ORAL::EP_CELL_NUMBER_IN_BALF;
  "% OF ALVEOLAR MACROPHAGES":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF;
  "% OF ALVEOLAR NEUTROPHILS":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF;
  "% OF ALVEOLAR EOSINOPHILS":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_PERC_IN_BALF;
  "% OF ALVEOLAR LYMPHOCYTES":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_PERC_IN_BALF;
  "NUMBER OF TOTAL ALVEOLAR MACROPHAGES IN BAL":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF;
  "NUMBER OF TOTAL ALVEOLAR NEUTROPHILS IN BAL":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF;
  "NUMBER OF TOTAL ALVEOLAR EOSINOPHILS IN BAL":
  result := HH_REPEATED_ORAL::EP_ALVEOLAR_EOSINOPHILS_NUMBER_IN_BALF;
  "NUMBER OF TOTAL ALVEOLAR LYMPHOCYTES IN BAL":
```

```
                    result := HH_REPEATED_ORAL::EP_ALVEOLAR_LYMPHOCYTES_NUMBER_IN_BALF
                  end;
                  "GENOTOXICITY":
                  case effectendpoint_s of
                  "DNA STRAND BREAKS":
                  result := HH_GENETIC_IN_VIVO::EP_DNA_STRAND_BREAKS
                end
              end
            end;
            HH_REPEATED_INHAL:
            begin
              case endpoint_s of
              "BALL ANALYSIS":
              case effectendpoint_s of
              "% OF ALVEOLAR MACROPHAGES":
              result := HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGE_PERC_IN_BALF;
              "% OF ALVEOLAR NEUTROPHILS":
              result := HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_PERC_IN_BALF;
              "NUMBER OF TOTAL ALVEOLAR MACROPHAGES IN BAL":
              result := HH_REPEATED_INHAL::EP_ALVEOLAR_MACROPHAGES_NUMBER_IN_BALF;
              "NUMBER OF TOTAL ALVEOLAR NEUTROPHILS IN BAL":
              result := HH_REPEATED_INHAL::EP_ALVEOLAR_NEUTROPHILS_NUMBER_IN_BALF
            end
          end
        end;
        HH_BARRIER_INTEGRITY:
        begin
          case endpoint_s of
            "EPITHELIAL INTEGRITY - TEER":
              result := HH_BARRIER_INTEGRITY::EP_INVITRO_BARRIER_INTEGRITY
          end;
          case effectendpoint_s of
          "TEER DECREASE VS CONTROL":
          result := HH_BARRIER_INTEGRITY::EP_TEER_DECREASE_VERSUS_CONTROL
        end
      end
  end
```

```
function EN_StudyResult.'Map ontology entry onto result endpoint descriptor'(category_endpoint :: any Enumeration,str : String ): any Enumerate
  case category_endpoint of
    PC_APPEARANCE:
      begin
        case str of
          "NPO_888":
            result := PC_APPEARANCE::EP_PHYSICAL_STATE
        end
          end;
        PC_SPECIFIC_SURFACE_AREA:
          begin
            case str of
              "ENM_0000091":
                begin
                  /* ENM_0000091 is not correctly specified, it should be volume specific surface area instead of specific surface area which is mass based.. */                    ;
                  result := PC_SPECIFIC_SURFACE_AREA::EP_VOLUME_SPECIFIC_SURFACE_AREA
                end;
              "CHEMINF_000515":
                begin
                  /* "CHEMINF_000515 can not be used to distinguish between MSSA or VSSA as it describes both of them.. " */                  ;
                  result := nil
                end
            end
          end;
        PC_ZETA_POTENTIAL:
          begin
            case str of
            "ENM_0000086":
            result := PC_ZETA_POTENTIAL::EP_ISOELECTRIC_POINT;
            "NPO_1302", "ENM_0000092":
            result := PC_ZETA_POTENTIAL::EP_ZETA_POTENTIAL
          end
      end;
      HH_GENETIC_IN_VITRO:
      begin
        case str of
        "ENM_0000040":
        result := HH_GENETIC_IN_VITRO::EP_DNA_STRAND_BREAKS;
        "ENM_0000068":
        /* VIABILITY => not clear, is this the effect endpoint cell viability of category cytotoxicity??  */
      end
    end
end
```

```
function EN_StudyResult.'Map onto operator type'(conditions : EN_Conditions ): DataOperator
  case effectendpoint_s of
    "MEDIAN":
      result := oMEDIAN;
    "MEAN", "AVERAGE":
      begin
        if (conditions ≠ nil) and conditions.HasQuantity_X() then
          result := oMEAN_XY
        else
          result := oMEAN
        end;
        "MODE":
        result := oMODE;
        "MODE2":
        result := oMODE_2nd;
        "AUC":
        result := oAUC;
        "SLOPE":
        result := oSLOPE;
        "NORMALIZED":
        result := oNORM;
        "PEAK":
        result := oPEAK
        else
        case effectendpoint_type_s of
        "MEDIAN":
        result := oMEDIAN;
        "MEAN", "AVERAGE":
        begin
          if (conditions ≠ nil) and conditions.HasQuantity_X() then
            result := oMEAN_XY
          else
            result := oMEAN
        end;
        "MODE":
        result := oMODE;
        "MODE2":
        result := oMODE_2nd;
        "AUC":
        result := oAUC;
        "SLOPE":
        result := oSLOPE;
        "NORMALIZED":
        result := oNORM;
        "PEAK":
        result := oPEAK
      end
  end


function EN_StudyResult.'Map onto enumerate'(endpoint_descriptor :: any Enumerate ): any Enumerate
  begin
    case endpoint_descriptor of
      PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D3_D1, PC_ASPECT_RATIO_SHAPE::EP_ASPECT_RATIO_D1_D3, PC_GRANULOMETRY::EP_FERET_DIAMETER_D1, PC_GRANULOMETRY::EP_FERET_DIAMETER_D3:
        begin
          /* For now these size measurements are considered to be related to the primary/constituent size */        ;
          result := slConstituentParticleLevel
        end
      end;
        if result = nil then
          case effectendpoint_s of    "IC10", "IC25", "IC50":
        result := IC_x;
      "EC10", "EC_20", "EC20 (48H)", "EC20 (72H)", "EC25", "EC25 (48H)", "EC25 (72H)", "EC50", "EC50 (48H)", "EC50 (72H)":
        result := EC_x;
      "IL-6 CONCENTRATION":
        result := BM_CYTOKINES::'IL-6';
      "TNF-A CONCENTRATION":
        result := BM_CYTOKINES::'TNF-A';
      "IL-10 CONCENTRATION":
        result := BM_CYTOKINES::'IL-10';
      "IL-12 CONCENTRATION":
        result := BM_CYTOKINES::'IL-12'
    end
  end
```

```
function EN_StudyResult.'Map onto value x'():Quantity
  begin
    case effectendpoint_s of
      "IC10", "EC10":
        result := 10.0·%;
      "EC20", "EC20 (48H)", "EC20 (72H)":
        result := 20.0·%;
      "IC25", "EC25":
        result := 25.0·%;
      "IC50", "EC50", "EC50 (48H)", "EC50 (72H)":
        result := 50.0·%
      end;
        case effectendpoint_type_s of
      "D10":
        result := 10.0·%;
      "D50":
        result := 50.0·%;
      "D90":
        result := 90.0·%
    end
  end


function EN_StudyResult.UnitFromEndpoint(src_unit :: Unit ):Unit
  begin
    result := src_unit;
    /* Some endpoints have the actual unit implicitly in their descriptor and the value expressed as unitless number */  ;
    if not Known(unit_s) or (unit_s = "") then
    begin
      case endpoint_s of
        "% CYTOTOXICITY", "% CELLULAR LDH/CONTROL", "% DECREASE AT MAX DOSE":
          begin
            result := ·%
          end
      end
    end
    else
    begin
      /* Some endpoints need to be corrected..  */    ;
      case effectendpoint_s of
        "NUMBER OF PARTICLES/CM3":
          result := ·cm⁻³
      end
    end
  end


function EN_StudyResult.'Map onto time t'():Quantity
  case effectendpoint_s of
    "EC20 (48H)", "EC25 (48H)", "EC50 (48H)":
      result := 48.0·h;
    "EC20 (72H)", "EC25 (72H)", "EC50 (72H)":
      result := 72.0·h
  end
```

Class `EN_StudiesRequest`

Defined composites

Any instance of `EN_StudiesRequest` is composed of

- at most one `response` of `EN_StudiesResponse`

Class `EN_StudiesResponse`

Defined composites

Any instance of `EN_StudiesResponse` is composed of

- zero or more `docs` of any kind of `EN_Study`

Class `EN_ParamsRequest`

Defined composites

Any instance of `EN_ParamsRequest` is composed of
- at most one `response` of EN_ParamsResponse

Class `EN_ParamsResponse`

Defined composites

Any instance of `EN_ParamsResponse` is composed of
- zero or more `docs` of EN_Params

Class `EN_Params`

”Aids used to disperse_s”:”N”,
”DISPERSION MEDIUM_s”:”no”,
”Dispersed in cell culture medium_s”:”In assay medium”,
”Dispersion technique used_s”:”Sonicating water bath”,
”Dispersion time duration_UNIT_s”:”min”,
”Dispersion time duration_d”:15.0,
”E.well_plate_UNIT_s”:”well plate”,
”E.well_plate_d”:96.0,
”Energy of sonication_s”:”unknown”,
”Operator_s”:”Anna Giusti”,
”Sonication-Bath_s”:”yes”,
”Total volume per well_UNIT_s”:”ml”,
”Total volume per well_d”:0.25,
”Vortexing_s”:”yes”,
”Additives used_s”:”no”
,”DISPERSION MEDIUM_s”:”Human Blood Serum (HBS)”
,”Dispersed in cell culture medium_s”:”no”
,”Dispersion time duration_UNIT_s”:”min”
,”Dispersion time duration_d”:1.0
,”E.method_s”:”FRAS”,
”E.sop_reference_s”:”https://dx.doi.org/10.1088/1742-6596/838/1/012033”
,”MEDIUM_s”:””
,”Operator_s”:”Kai Werle”
,”SERUM_s”:”% 100 HBS”
,”Sonication-Bath_UNIT_s”:”min”
,”Sonication-Bath_d”:1.0
,”document_uuid_s”:”GRCS-e713def0-88b3-4a56-ae2d-56e5f42209e7”
,”endpointcategory_s”:”RADICAL_FORMATION_POTENTIAL_SECTION”
,”guidance_s”:”JOURNAL OF PHYSICS: CONF. SERIES 838 (2017) 012033”
,”id”:”GRCS-e713def0-88b3-4a56-ae2d-56e5f42209e7/3776/prm”
,”topcategory_s”:”P-CHEM”
,”type_s”:”params”

Attributes

name	type	domain	inference	comment
'Lead scientist_s'	: String			
MEDIUM_s	: String			
'MEDIUM.composition_s'	: String			
'MEDIUM.ph_d'	: Real			
'MEDIUM.temperature_UNIT_s'	: String			
'MEDIUM.temperature_d'	: Real			
'MEDIUM.CO2_concentration_UNIT_s'	: String			
'MEDIUM.CO2_concentration_d'	: Real			
'MEDIUM.O2_concentration_UNIT_s'	: String			
'MEDIUM.O2_concentration_d'	: Real			
'MEDIUM.ionic_strength_UNIT_s'	: String			
'MEDIUM.ionic_strength_d'	: Real			
'material state_s'	: String			
'Dispersion protocol_s'	: String			
'DISPERSION MEDIUM_s'	: String			
'Dispersion/dilution medium_s'	: String			
'Dispersion time duration_d'	: Real			
'Dispersion time duration_UNIT_s'	: String			

'E.positive_control_id_s'	: String			
'E.positive_control2_id_s'	: String			
'E.positive_control_concentration_unit_s'	: String			
'E.positive_control_concentration_d'	: Real			
'E.sop_reference_s'	: String			
'T.instrumentmodel_s'	: String			
'T.sampleweight_d'	: Real			
'T.sampleweight_UNIT_s'	: String			
'T.temperature_d'	: Real			
'T.temperature_UNIT_s'	: String			
'Amount of powder_d'	: Real			
'Amount of powder_UNIT_s'	: String			
'SERUM_s'	: String			
'E.cell_source_s'	: String			
'T.Cell model_s'	: String			
'E.cell_type_s'	: String			
'E.days_of_differentiation_UNIT_s'	: String			
'E.days_of_differentiation_d'	: Real			
'E.exposure_system_s'	: String			
'E.exposure_time_UNIT_s'	: String			
'E.exposure_time_d'	: Real			
'E.incubation_time_before_exposure_UNIT_s'	: String			
'E.incubation_time_before_exposure_d'	: Real			
'T.AEROSOLISATION_ASSAY_NAME_s'	: String			
'T.AEROSOLISATION_EXPOSURE_SYSTEM_s'	: String			
'T.AEROSOLISATION_INSTRUMENT_s'	: String			
'T.AEROSOLISATION_METHOD_s'	: String			
'T.ABSORBENTGAS_s'	: String			
'T.ANALYSIS_POINTS_s'	: String			
'T.DEGASSING_RAMP_s'	: String			
'T.START_RELATIVE_PRESSURE_s'	: String			
'T.END_RELATIVE_PRESSURE_s'	: String			
'T.INSTRUMENT_MANUFACTURER_s'	: String			
'T.INSTRUMENT_MODEL_s'	: String			
'T.INSTRUMENT_TYPE_s'	: String			
'T.OUTGASSING_TEMP_s'	: String			
'T.OUTGASSING_TIME_s'	: String			
'T.SAMPLE_WEIGHT_s'	: String			
'SAMPLE_PREPARATION.Final sample concentration_ UNIT_s'	: String			
'SAMPLE_PREPARATION.Final sample concentration_d'	: Real			
'Lot/Batch no._s'	: String			

'Operator_s'	: String			

Operators

```
function EN_Params.MapTo_MediumDescriptor(): MediumDescriptor
  begin
    if Known(MEDIUM_s) then
      result := MapMediumStr(MEDIUM_s)  ;
    if (result = nil) and Known('DISPERSION MEDIUM_s') then
      result := MapMediumStr('DISPERSION MEDIUM_s')
  end


function EN_Params.MapTo_CellType(): any Enumerate
  if Known('E.cell_type_s') then
    result := MapCellTypeStr('E.cell_type_s')
```

Class `EN_ConditionsRequest`

Defined composites

Any instance of `EN_ConditionsRequest` is composed of
- at most one `response` of `EN_ConditionsResponse`

Class `EN_ConditionsResponse`

Defined composites

Any instance of `EN_ConditionsResponse` is composed of
- zero or more `docs` of `EN_Conditions`

Class EN_Conditions

Attributes

name	type	domain	inference	comment
pH_d	: Real			
effectid_hs	: String			*Refers to study id this condition belongs to*
'Sample name_s'	: String			
'E.exposure_time_UNIT_s'	: String			
'E.exposure_time_d'	: Real			
'E.exposure_time_s'	: String			
'concentration_UNIT_s'	: String			
'concentration_d'	: Real			
'concentration_s'	: String			
'concentration_mass_UNIT_s'	: String			
'concentration_mass_d'	: Real			
'concentration_ml_UNIT_s'	: String			
'concentration_ml_d'	: Real			
'dose_UNIT_s'	: String			
'dose_d'	: Real			
'mass-to-charge ratio_UNIT_s'	: String			
'mass-to-charge ratio_d'	: Real			
'replicate_s'	: String			
'replicate_d'	: Real			
'Technical replicate_s'	: String			
'Biological replicate_s'	: String			
'Experiment_s'	: String			*"Experiment_s":"Experiment 2"*
'Treatment_s'	: String			
'material_s'	: String			
'E.cell_type_s'	: String			
element_or_group_s	: String			
'gender_s'	: String			
'E.animal_model_s'	: String			
'size_measurement_s'	: String			
'size_measurement_type_s'	: String			

Operators

```
function EN_Conditions.HasQuantity_X(): Boolean
| Known('concentration_d') or Known('concentration_mass_d') or Known('concentration_ml_d') or Known('dose_d')
```

```
function EN_Conditions.MapQuantities_X(): UReals
  begin
    if Known('concentration_d') then
      with MapUnitStr('concentration_UNIT_s') | conc_unit then
        result→Add('concentration_d'→WithUnit(conc_unit))  ;
    if Known('concentration_mass_d') then
      with MapUnitStr('concentration_mass_UNIT_s') | conc_unit then
        result→Add('concentration_mass_d'→WithUnit(conc_unit))  ;
    if Known('concentration_ml_d') then
      with MapUnitStr('concentration_ml_UNIT_s') | conc_unit then
        result→Add('concentration_ml_d'→WithUnit(conc_unit))  ;
    if Known('dose_d') then
      with MapUnitStr('dose_UNIT_s') | dose_unit then
        result→Add('dose_d'→WithUnit(dose_unit))
  end
```

8.2 Defined collections

EN_Substances defines a sequence containing EN_Substance objects.
EN_StudyResults defines a sequence containing EN_StudyResult objects.
EN_Constituents defines a sequence containing EN_Composition objects.
EN_Studies defines a sequence containing any kind of EN_Study objects.

Defined expressions

name	type	expression	comment
baseurl	: String	BaseUrl()	
auth_key	: String	OAuth2Key()	

Operators

```
function ENANOMAPPER_FED_KB::getSubstances() :: EN_Substances
  with RESTQuery(baseurl, auth_key, "select?q=*:*&fq=type_s:substance&rows=1000&wt=json", EN_SubstancesRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs;
      resp→RemoveAllComponents(docs)
    end


function ENANOMAPPER_FED_KB::getSubstancesString() :: String
| RESTQuery(baseurl, auth_key, "select?q=*:*&fq=type_s:substance&rows=1&wt=json", String)


function ENANOMAPPER_FED_KB::getIdentifierString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_hs:" + substanceID + "&fq=type_s:identifier&wt=json", String)


function ENANOMAPPER_FED_KB::getComposition( substanceID : String ) :: EN_Constituents
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_hs:" + substanceID + "&fq=type_s:composition&rows=1000&wt=json", EN_CompositionRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs;
      resp→RemoveAllComponents(docs)
    end


function ENANOMAPPER_FED_KB::getCompositionString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_hs:" + substanceID + "&fq=type_s:composition&rows=1000&wt=json", String)
```

```
function ENANOMAPPER_FED_KB::getStudiesResults( substanceID : String ) :: EN_StudyResults
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&rows=1000&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs;
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudiesResultsString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&rows=1000&wt=json", String)

function ENANOMAPPER_FED_KB::getStudyResults( documentID : String ) :: EN_StudyResults
  with RESTQuery(baseurl, auth_key, "select?q=document_uuid_s:" + documentID + "&fq=type_s:study&rows=1000&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs;
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudyResultsString( documentID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=document_uuid_s:" + documentID + "&fq=type_s:study&rows=1000&wt=json", String)

function ENANOMAPPER_FED_KB::getSubstance( substanceID : String ) :: EN_Substance
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_hs:" + substanceID + "&fq=type_s:substance&wt=json", EN_SubstancesRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs[1];
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getSubstanceString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_hs:" + substanceID + "&fq=type_s:substance&wt=json", String)

function ENANOMAPPER_FED_KB::getStudyDocumentIDs( substanceID : String ) :: Strings
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&fl=document_uuid_s&rows=1000&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      req→RemoveComponent(response, resp);
      result := resp.docs.document_uuid_s→Unique
    end

function ENANOMAPPER_FED_KB::getStudyDocumentIDsString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&fl=document_uuid_s&rows=1000&wt=json", String)

function ENANOMAPPER_FED_KB::getStudies( substanceID : String ) :: EN_Studies
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&rows=1000&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      foreach en_study of resp.docs do
        if not result→Exists(en_st | en_st.document_uuid_s = en_study.document_uuid_s) then
          result→Add(en_study)    ;
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudiesString( substanceID : String ) :: String
| RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study&rows=1000&wt=json", String)
```

```
function ENANOMAPPER_FED_KB::getStudyResult(studyID : String ):: EN_StudyResult
  with RESTQuery(baseurl, auth_key, "select?q=id:" + studyID + "&fq=type_s:study&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs[1];
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getAppearanceInformation(substanceID : String ):: EN_StudyResults
  with RESTQuery(baseurl, auth_key, "select?q=s_uuid_s:" + substanceID + "&fq=type_s:study &fq=endpoint_s:APPEARANCE&rows=1000&wt=json", EN_StudiesResultsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs;
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudyParams(documentID : String ):: EN_Params
  with RESTQuery(baseurl, auth_key, "select?q=document_uuid_s:" + documentID + "&fq=type_s:params&rows=1&wt=json", EN_ParamsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs→If(docs | docs[1], nil);
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudyParamsString(documentID : String ):: String
| RESTQuery(baseurl, auth_key, "select?q=document_uuid_s:" + documentID + "&fq=type_s:params&rows=1&wt=json", String)

function ENANOMAPPER_FED_KB::getStudyResultConditions(effectID : String ):: EN_Conditions
  with RESTQuery(baseurl, auth_key, "select?q=effectid_hs:" + effectID + "&fq=type_s:conditions&rows=1000&wt=json", EN_ConditionsRequest) | req then
    with req.response | resp then
    begin
      result := resp.docs→If(docs | docs[1], nil);
      resp→RemoveAllComponents(docs)
    end

function ENANOMAPPER_FED_KB::getStudyResultConditionsString(effectID : String ):: String
| RESTQuery(baseurl, auth_key, "select?q=effectid_hs:" + effectID + "&fq=type_s:conditions&rows=1000&wt=json", String)
```

```
function ENANOMAPPER_FED_KB::MapUnitStr( str : String ):: Unit
  case str→Trim of
    "":
      result := Real;
    "%", "%v/v", "%w/w", "wt%", "at%", "% DNA IN TAIL", "%DNA in Tail", "% tail":
      result := ·%;
    "m":
      result := ·m;
    "cm":
      result := ·cm;
    "um", "micron":
      result := ·µm;
    "nm":
      result := ·nm;
    "/day":
      result := ·d⁻¹;
    "1/mg":
      result := ·mg⁻¹;
    "Celsius":
      result := ·°C;
    "cm/s":
      result := ·cm·s⁻¹;
    "cm^3":
      result := ·cm³;
    "day", "d":
      result := ·d;
    "g":
      result := ·g;
    "ug":
      result := ·µg;
    "°":
      result := ·°;
    "g/cm3", "g/cm^3":
      result := ·g·cm⁻³;
    "g/l":
      result := ·g·l⁻¹;
    "g/mL":
      result := ·g·ml⁻¹;
    "ng/ml":
      result := ·ng·ml⁻¹;
    "ng/cm2/h":
      result := ·ng·cm⁻²·h⁻¹;
    "ug/cm2":
      result := ·µg·cm⁻²;
    "ug/l":
      result := ·µg·l⁻¹;
    "ug/ml":
      result := ·µg·ml⁻¹;
    "h", "hour":
      result := ·h;
    "m2/cm3":
      result := ·m²·cm⁻³;
    "m2/g":
      result := ·m²·g⁻¹;
    "m2/l":
      result := ·m²·l⁻¹;
    "mg/l", "mg /L", "mg/L":
      result := ·mg·l⁻¹;
    "mg/dl":
      result := ·mg·dl⁻¹;
    "mg/kg":
      result := ·mg·kg⁻¹;
    "mg/ml", "mg/mL":
      result := ·mg·ml⁻¹;
    "mg/m^3":
      result := ·mg·m⁻³;
    "cm3/g":
      result := ·cm³·g⁻¹;
    "millisecond":
      result := ·ms;
    "min", "minute":
      result := ·min;
    "ml":
```

```
    result := ·ml;
  "ml/g":
    result := ·ml·g⁻¹;
  "mV":
    result := ·mV;
  "mM(10^-3 mol)/kg":
    result := ·mmol·kg⁻¹;
  "mM(10^-3 mol)/L":
    result := ·mmol·l⁻¹;
  "nM(10^-9 mol)/L":
    result := ·nmol⁻¹;
  "nmol/ml":
    result := ·nmol·ml⁻¹;
  "ohms/cm2":
    result := Ω··cm⁻²;
  "particles/L":
    result := ·l⁻¹;
  "pg/ml":
    result := ·pg·ml⁻¹;
  "ppb":
    result := ·ppb;
  "ppm":
    result := ·ppm;
  "uM(10^-6 mol)":
    result := ·µmol;
  "uM(10^-6 mol)/kg":
    result := ·µmol·kg⁻¹;
  "mM":
    result := ·mmol·l⁻¹;
  "uM(10^-6 mol)/L", "µM", "uM":
    result := ·µmol·l⁻¹;
  "um^2":
    result := ·µm²;
  "nmol TEU/L":
    result := ·nmol·l⁻¹;
  "AU", "AU (ex/em 480/530)":
    result := ·AU;
  "O.D.":
    result := ·OD;
  "Ω":
    result := Ω·;
  "Ω cm^2", "Ω cm^2":
    result := Ω··cm⁻²;
  "kJ mol-1":
    result := ·kJ·mol⁻¹;
  "J mol-1 K-1":
    result := ·J·mol⁻¹·K⁻¹
 end

function ENANOMAPPER_FED_KB::MapDistrQualifierFromStr(str : String):: DistrQualifier
 case str of
  "RSD %":
    result := dqRSD_PERC;
  "sd", "SD":
    result := dqSD;
  "±":
    result := dqPLUS_MIN
 end
```

```
function ENANOMAPPER_FED_KB::MapTimeS( str : String ) :: Quantity
  with str→Trim | s then
  begin
    case s of
      "time 0":
        result := 0.0·s;
      "24 h":
        result := 24.0·h;
      "48 h":
        result := 48.0·h;
      "72 h":
        result := 72.0·h;
      "7 day":
        result := 7.0·d;
      "10 day":
        result := 10.0·d;
      "14 day":
        result := 14.0·d;
      "17 day":
        result := 17.0·d;
      "21 day":
        result := 21.0·d
      else
        result := 0.0
    end
  end
  else
    result := 0.0

function ENANOMAPPER_FED_KB::MapMediumStr( str : String ) :: any Enumerate
  case str→Trim of
    "Inhalation: lung lining simulant fluid (LSF)":
      result := 'Simulated lung airway lining fluid';
    "Oral & Inhalation: Lysosomal simulant fluid (PSF)", "lysosome":
      result := 'Simulated lung macrophage phagolysosomal fluid';
    "deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2":
      result := 'deionized water containing 50 mM DMPO, 0.001 mM FeSO4 and 0.01 mM H2O2';
    "Milli-Q Water":
      result := 'Ultra pure water';
    "Human Blood Serum (HBS)":
      result := 'Human blood serum (HBS)'
  end
```

```
function ENANOMAPPER_FED_KB::MapCellTypeStr( str : String ):: any Enumerate
  case str→Trim of
    "HEK293":
      result := 'HEK293 (human embryonic kidney cell line)';
    "A549":
      result := 'A549 (human alveolar cell line)';
    "CALU-3":
      result := 'Calu-3 (human bronchial cell line)';
    "CACO-2":
      result := 'CACO-2 (human cell line)';
    "THP-1":
      result := 'THP-1 (human leukemic monocyte cell line)';
    "TK6":
      result := 'TK6 (human lymphoblastoid cells)';
    "BEAS-2B", "Beas 2b":
      result := 'BEAS-2B (human lung epithelial cells)';
    "RAW 264.7":
      result := 'RAW 264.7 (mouse macrophages cell line)';
    "V79":
      result := 'V79 (chinese hamster)';
    "3T3":
      result := '3T3 (mouse embryonic fibroblasts)';
    "carp leukocyte cell line":
      result := 'carp leukocyte cell line';
    "Kupffer cells":
      result := 'Kupffer cells';
    "Hep3B":
      result := 'Hep3B (human)';
    "Caki-1":
      result := 'Caki-1 (human cell line)';
    "NRK-52e":
      result := 'NRK-52E (rat, normal kidney cell line)'
  end

function ENANOMAPPER_FED_KB::MapQuantity( unit_str : String, d : Real ):: Quantity
  with MapUnitStr(unit_str) | u then
    result := d→WithUnit(u)
  else
    result := 0.0
```

Chapter 9 ECHA_USE_KB

9.1 Defined enumerations

LCS

REACH Table R.12- 8: Descriptor list for Life cycle stages (LCS)

- `LCS_M`
  Manufacture
- `LCS_F`
  Formulation or re-packing
- `LCS_IS`
  Use at industrial sites
- `LCS_PW`
  Widespread use by professional workers
- `LCS_C`
  Consumer use
- `LCS_SL`
  Service life

PC

REACH Table R.12- 10: Descriptor list for Product Categories (PC)

- `PC1`
  Adhesives, sealants
- `PC2`
  Adsorbents
- `PC3`
  Air care products
- `PC4`
  Anti-Freeze and de-icing products
- `PC7`
  Base metals and alloys
- `PC8`
  Biocidal products
- `PC9a`
  Coatings and paints, thinners, paint removers
- `PC9b`
  Fillers, putties, plasters, modelling clay
- `PC9c`
  Finger paints
- `PC11`
  Explosives
- `PC12`
  Fertilizers
- `PC13`
  Fuels
- `PC14`
  Metal surface treatment products
- `PC15`
  Non-metal-surface treatment products
- `PC16`
  Heat transfer fluids
- `PC17`
  Hydraulic fluids
- `PC18`
  Ink and toners
- `PC20`
  Processing aids such as pH-regulators, flocculants, precipitants, neutralization agents

- PC21
  Laboratory chemicals
- PC23
  Leather treatment products
- PC24
  Lubricants, greases, release products
- PC25
  Metal working fluids
- PC26
  Paper and board treatment products
- PC27
  Plant protection products
- PC28
  Perfumes, fragrances
- PC29
  Pharmaceuticals
- PC30
  Photo-chemicals
- PC31
  Polishes and wax blends
- PC32
  Polymer preparations and compounds
- PC33
  Semiconductors
- PC34
  Textile dyes, and impregnating products
- PC35
  Washing and cleaning products
- PC36
  Water softeners
- PC37
  Water treatment chemicals
- PC38
  Welding and soldering products, flux products
- PC39
  Cosmetics, personal care products
- PC40
  Extraction agents
- PC41
  Oil and gas exploration or production products
- PC42
  Electrolytes for batteries
- PC0
  Other

PROC

REACH Table R.12- 11: Descriptor list for Process Categories (PROC)

- PROC1
  Chemical production or refinery in closed process without likelihood of exposure or processes with equivalent containment conditions.
- PROC2
  Chemical production or refinery in closed continuous process with occasional controlled exposure or processes with equivalent containment conditions
- PROC3
  Manufacture or formulation in the chemical industry in closed batch processes with occasional controlled exposure or processes with equivalent containment condition
- PROC4
  Chemical production where opportunity for exposure arises
- PROC5
  Mixing or blending in batch processes
- PROC6
  Calendering operations
- PROC7
  Industrial spraying

- PROC8a
  Transfer of substance or mixture (charging and discharging) at nondedicated facilities
- PROC8b
  Transfer of substance or mixture (charging and discharging) at dedicated facilities
- PROC9
  Transfer of substance or mixture into small containers (dedicated filling line, including weighing)
- PROC10
  Transfer of substance or mixture into small containers (dedicated filling line, including weighing)
- PROC11
  Non industrial spraying
- PROC12
  Use of blowing agents in manufacture of foam
- PROC13
  Treatment of articles by dipping and pouring
- PROC14
  Tabletting, compression, extrusion, pelletisation, granulation
- PROC15
  Use as laboratory reagent
- PROC16
  Use of fuels
- PROC17
  Lubrication at high energy conditions in metal working operations
- PROC18
  General greasing /lubrication at high kinetic energy conditions
- PROC19
  Manual activities involving hand contact
- PROC20
  Use of functional fluids in small devices
- PROC21
  Low energy manipulation and handling of substances bound in/on materials or articles
- PROC22
  Manufacturing and processing of minerals and/or metals at substantially elevated temperature
- PROC23
  Open processing and transfer operations at substantially elevated temperature
- PROC24
  High (mechanical) energy work-up of substances bound in /on materials and/or articles
- PROC25
  Other hot work operations with metals
- PROC26
  Handling of solid inorganic substances at ambient temperature
- PROC27a
  Production of metal powders (hot processes)
- PROC27b
  Production of metal powders (wet processes)
- PROC28
  Manual maintenance (cleaning and repair) of machinery
- PROC0
  Other

ERC

REACH Table R.12- 13: Descriptor list for Environmental Release Categories (ERC)

- ERC1
  Manufacture of the substance
- ERC2
  Formulation into mixture
- ERC3
  Formulation into solid matrix
- ERC4
  Use of non-reactive processing aid at industrial site (no inclusion into or onto article)
- ERC6b
  Use of reactive processing aid at industrial site (no inclusion into or onto article)

- ERC6a
  Use of intermediate
- ERC6c
  Use of monomer in polymerisation processes at industrial site (inclusion or not into/onto article)
- ERC6d
  Use of reactive process regulators in polymerisation processes at industrial site (inclusion or not into/onto article)
- ERC5
  Use at industrial site leading to inclusion into/onto article
- ERC7
  Use of functional fluid at industrial site
- ERC8a
  Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor)
- ERC8d
  Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor)
- ERC8b
  Widespread use of reactive processing aid (no inclusion into or onto article, indoor)
- ERC8e
  Widespread use of reactive processing aid (no inclusion into or onto article, outdoor)
- ERC8c
  Widespread use leading to inclusion into/onto article (indoor)
- ERC8f
  Widespread use leading to inclusion into/onto article (outdoor)
- ERC9a
  Widespread use of functional fluid (indoor)
- ERC9b
  Widespread use of functional fluid (outdoor)
- ERC10a
  Widespread use of articles with low release (outdoor)
- ERC11a
  Widespread use of articles with low release (indoor)
- ERC10b
  Widespread use of articles with high or intended release (outdoor)
- ERC11b
  Widespread use of articles with high or intended release (indoor)
- ERC12a
  Processing of articles at industrial sites with low release
- ERC12b
  Processing of articles at industrial sites with high release
- ERC12c
  Use of articles at industrial sites with low release

AC

REACH Table R.12- 14: Descriptor list for Articles Categories (AC)

- AC1
  Vehicles
- AC1a
  Vehicles covered by End of Life Vehicles (ELV) directive
- AC1b
  Other vehicles
- AC2
  Machinery, mechanical appliances, electrical/electronic articles
- AC2a
  Machinery, mechanical appliances, electrical/electronic articles covered by the Waste Electrical and Electronic Equipment (WEEE) directive
- AC2b
  Other machinery, mechanical appliances, electrical/electronic articles
- AC3
  Electrical batteries and accumulators
- AC4
  Stone, plaster, cement, glass and ceramic articles
- AC4a
  Stone, plaster, cement, glass and ceramic articles: Large surface area articles

- AC4b
  Stone, plaster, cement, glass and ceramic articles: Toys intended for children's use (and child dedicated articles)
- AC4c
  Stone, plaster, cement, glass and ceramic articles: Packaging (excluding food packaging)
- AC4d
  Stone, plaster, cement, glass and ceramic articles: Articles intended for food contact
- AC4e
  Stone, plaster, cement, glass and ceramic articles: Furniture & furnishings
- AC4f
  Stone, plaster, cement, glass and ceramic articles: Articles with intense direct dermal contact during normal use
- AC4g
  Other articles made of stone, plaster, cement, glass or ceramic
- AC5
  Fabrics, textiles and apparel
- AC5a
  Fabrics, textiles and apparel: Large surface area articles
- AC5b
  Fabrics, textiles and apparel: Toys intended for children's use (and child dedicated articles)
- AC5c
  Fabrics, textiles and apparel: Packaging (excluding food packaging)
- AC5d
  Fabrics, textiles and apparel: Articles intended for food contact
- AC5e
  Fabrics, textiles and apparel: Furniture & furnishings, including furniture coverings
- AC5f
  Fabrics, textiles and apparel: Articles with intense direct dermal contact during normal use
- AC5g
  Fabrics, textiles and apparel: Articles with intense direct dermal contact during normal use: bedding and mattresses
- AC5h
  Other articles made of fabrics, textiles and apparel
- AC6
  Leather articles
- AC6a
  Leather articles: Large surface area articles
- AC6b
  Leather articles: Toys intended for children's use (and child dedicated articles)
- AC6c
  Leather articles: Packaging (excluding food packaging)
- AC6d
  Leather articles: Articles intended for food contact
- AC6e
  Leather articles: Furniture & furnishings, including furniture coverings
- AC6f
  Leather articles: Articles with intense direct dermal contact during normal use
- AC6g
  Other leather articles
- AC7
  Metal articles
- AC7a
  Metal articles: Large surface area articles
- AC7b
  Metal articles: Toys intended for children's use (and child dedicated articles)
- AC7c
  Metal articles: Packaging (excluding food packaging)
- AC7d
  Metal articles: Articles intended for food contact
- AC7e
  Metal articles: Furniture & furnishings
- AC7f
  Metal articles: Articles with intense direct dermal contact during normal use
- AC7g
  Other metal articles
- AC8
  Paper articles

- AC8a
  Paper articles: Large surface area articles
- AC8b
  Paper articles: Toys intended for children's use (and child dedicated articles)
- AC8c
  Paper articles: Packaging (excluding food packaging)
- AC8d
  Paper articles: Articles intended for food contact
- AC8e
  Paper articles: Furniture & furnishings
- AC8f1
  Paper articles: Articles with intense direct dermal contact during normal use: personal hygiene articles
- AC8f2
  Paper articles: Articles with intense direct dermal contact during normal use: printed articles with dermal contact in normal conditions of use
- AC8g
  Other paper articles
- AC10
  Rubber articles
- AC10a
  Rubber articles: Large surface area articles
- AC10b
  Rubber articles: Toys intended for children's use (and child dedicated articles)
- AC10c
  Rubber articles: Packaging (excluding food packaging)
- AC10d
  Rubber articles: Articles intended for food contact
- AC10e
  Rubber articles: Furniture & furnishings, including furniture coverings
- AC10f
  Rubber articles: Articles with intense direct dermal contact during normal use
- AC10g
  Other rubber articles
- AC11
  Wood articles
- AC11a
  Wood articles: Large surface area articles
- AC11b
  Wood articles: Toys intended for children's use (and child dedicated articles)
- AC11c
  Wood articles: Packaging (excluding food packaging)
- AC11d
  Wood articles: Articles intended for food contact
- AC11e
  Wood articles: Furniture & furnishings
- AC11f
  Wood articles: Articles with intense direct dermal contact during normal use
- AC11g
  Other wood articles
- AC13
  Plastic articles
- AC13a
  Plastic articles: Large surface area articles
- AC13b
  Plastic articles: Toys intended for children's use (and child dedicated articles)
- AC13c
  Plastic articles: Packaging (excluding food packaging)
- AC13d
  Plastic articles: Articles intended for food contact
- AC13e
  Plastic articles: Furniture & furnishings, including furniture coverings
- AC13f
  Plastic articles: Articles with intense direct dermal contact during normal use
- AC13g
  Other plastic articles

- AC0
  Other

SU

Table R.12- 9: Descriptor list for Sectors of use (SU)

- SU1
  Agriculture, forestry, fishery
- SU2a
  Mining, (without offshore industries)
- SU2b
  Offshore industries
- SU4
  Manufacture of food products
- SU5
  Manufacture of textiles, leather, fur
- SU6a
  Manufacture of wood and wood products
- SU6b
  Manufacture of pulp, paper and paper products
- SU7
  Printing and reproduction of recorded media
- SU8
  Manufacture of bulk, large scale chemicals (including petroleum products)
- SU9
  Manufacture of fine chemicals
- SU11
  Manufacture of rubber products
- SU12
  Manufacture of plastics products, including compounding and conversion
- SU13
  Manufacture of other non-metallic mineral products, e.g. plasters, cement
- SU14
  Manufacture of basic metals, including alloys
- SU15
  Manufacture of fabricated metal products, except machinery and equipment
- SU16
  Manufacture of computer, electronic and optical products, electrical equipment
- SU17
  General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment
- SU18
  Manufacture of furniture
- SU19
  Building and construction work
- SU20
  Health services
- SU23
  Electricity, steam, gas water supply and sewage treatment
- SU24
  Scientific research and development
- SU0
  Other

TF

- 'Ablative'
  Substance that is applied to a substrate to protect it from heat by dissipating heat through the process of erosion, melting, or vaporization of the material.
- 'Abrasive'
  An abrasive is a substance used to abrade, smooth, or polish an object. Abrasives are used to remove imperfections from a surface; used to smooth, scour, scrub, clean, wear down, or polish surfaces by rubbing against the surface; usually fine powders of hard substances. Examples include sandstones, pumice, quartz, silicates, aluminium oxides, and glass.
- 'Absorbent'
  Chemical substance used to retain other substances by assimilation.

- 'Aerating and dearating agents'
  Substance that influences the amount of air or gases entrained in a material.
- 'Antiadhesive'
  Substance that prevents or reduces the adhesion of a material to itself or to another material; prevents bonding between other substances by discouraging surface attachment; functions as the antitheses of adhesive.
- 'Alloying element'
  Substances that are added to metals alloys like steel to modify its properties such as strength, hardness, or to facilitate its treatment.
- 'Anticaking agent'
  Substance that prevents granular or particulate materials from sticking or caking during transfer, storage, or use.
- 'Anticondensation agent '
  Substance or material that is used to avoid condensation on surfaces and in the atmosphere.
- 'Antifreeze agent'
  A substance added to fluids, especially water, to reduce the freezing point of the mixture, or applied to surfaces to melt or prevent the build-up of ice. Examples of products include antifreeze liquids, windshield de-icers, aircraft de-icers, lock release agents, ice melting crystals, and rock salt.
- 'Antioxidant'
  Substance that retards oxidation, rancidity, deterioration, and gum formation; used to maintain the quality, integrity, and safety of finished products by inhibiting the oxidative degradation of the ingredients in the formulation. Saturated polymers have greater oxidative stability and require relatively low concentrations of stabilizers.
- 'Antiredeposition agent'
  Any substance that prevents dirt and grease from resettling on a cleaned surface or that helps keep soils from re-depositing onto clothing in the wash water after they have been removed. Antiredeposition agents are water-soluble and typically negatively charged.
- 'Antiscaling agent'
  Substances added to products to prevent the build-up of inorganic oxide deposits. The formation of scale can be caused by the deposition of salts or minerals and may not necessarily lead to surface corrosion, therefore these chemicals are not corrosion inhibitors. Substances prevent the build-up or removes limescale and fouling. These substances are also called 'Descalers'.
- 'Antistatic agent'
  Any substance that prevents or reduces the tendency of a material to accumulate a static charge or alters the electrical properties of materials by reducing their tendency to acquire an electrical charge.
- 'Antistreaking agent'
  A substance which serves to enhance evaporation or reduce film formation in order to prevent the formulation of streaks on a surface during cleaning.
- 'Barrier (Sealant)'
  Material designed only to fill up a space, prevent seepage of moisture or air, passage of liquid or gas. The spaces can be joints, gaps or cavities that occur between two substrates.
- 'Binder'
  Any cementitious material that is used to hold dry powders or aggregate together; added to compounded dry powder mixtures of solids to provide adhesive qualities during and after compression to make tablets or cakes; is soft at high temperatures and hard at room temperature.
- 'Biocide'
  Substance intended for preventing, neutralizing, destroying, repelling, or mitigating the effects of any pest or microorganism; that inhibits the growth, reproduction, and activity of organisms, including fungal cells; decreases the number of fungi or pests present; deters microbial growth and degradation of other ingredients in the formulation.
- 'Bleaching agent'
  A bleaching agent is a material that lightens or whitens a substrate through chemical reaction. The bleaching reactions usually involve oxidative or reductive processes that degrade colour systems. Bleaching and decolourization can occur by destroying one or more of the double bonds in the conjugated chain, by cleaving the conjugated chain, or by oxidation of one of the other moieties in the conjugated chain.
- 'Brightener'
  Substance that is used to brighten, whiten, or enhance the appearance of colour of fabric and paper, usually by absorbing light in the ultraviolet and violet region (340-370 nm) of the electromagnetic spectrum, and re-emitting light in the blue region (420-470 nm). This causes a "whitening" effect by increasing the overall amount of blue light reflected. Optically colourless on the substrate and do not absorb in the visible part of the spectrum.
- 'Catalyst'
  Substances that increase the efficiency of a chemical reaction e.g. reaction needs less energy. Catalysts take part in the reaction but are not consumed during the process.
- 'Chain transfer agent'
  Substance that terminates the growth of a molecular chain and forms a new radical that can act as the initiator for a new chain.
- 'Chelating agent'
  A substance that has the ability to complex with inactivate metallic ions; used to remove ions from solutions and soils by forming a type of coordination complex so that the ions usual precipitation reactions are prevented; material that cleans oxide films from metals by stabilizing metal ions through complexing heterocyclic rings around each ion. They contain two or more electron donor atoms that can form coordinate bonds to a single metal atom. After the first such coordinate bond, each successive donor atom that binds creates a ring containing the metal atom; this cyclic structure is called a chelation complex or chelate.
- 'Cleaning agent'
  Substance or material used to remove dirt or impurities from surfaces; acts to loosen and remove dirt and grease from surfaces.
- 'Cloud-point depressant'
  Substance that depresses the temperature at which solids begin to separate from a liquid, at a temperature lower than that normally allowed.
- 'Coalescing agent'
  Ingredients that decrease the minimum film-forming temperature (MFT) and, upon evaporation, yield a hard film. In polishes, the most common coalescing agent is glycol ether however, pyrrolidines and benzoates are also used.
- 'Compatibilizer'
  Enables a reaction between two or more dissimilar polymers, allowing them to become more intimately mixed than before.
- 'Conductive agent'
  Material used to conduct electrical current.
- 'Corrosion inhibitor'
  Chemical substance used to prevent or retard corrosion metallic materials. They are needed in many products packaged in metal containers (such as aerosol products) and also used in such products as lubricants and other metal treatment products to provide protection to the substrates or surfaces on which the lubricants are used.
- 'Crystal growth modifiers (nucleating agents)'
  Substance used to reduce or increase crystal growth.
- 'Deflocculant'
  Substance used to fluidize concentrated slurries to reduce their bulk viscosity or stickiness in processing or handling.
- 'Defoamer'
  Chemical that is used to control foam; prevents foam from forming; breaks down any foam that does form; reduces foaming from proteins, gases, or nitrogenous materials. They reduce the tendency of finished products to generate foam on shaking or agitation. The ability of a material to act as an antifoam depends on its tendency to concentrate on the surface of existing or forming bubbles and to disrupt the continuous films of liquid surrounding them. As process aid, it improves filtration, dewatering, washing, and drainage of many types of suspensions, mixtures, and slurries.

- 'Demulsifier'
  Substance used to destroy an emulsion or prevent its formation.
- 'Density modifier'
  Substance that modifies the density of a material.
- 'Deodorizer'
  Substance that reduces or eliminates unpleasant odour and protects against the formation of malodour on body surfaces. Counteraction, sometimes referred to as neutralization, occurs when two odorous substances are mixed in a given ratio and the resulting odour of the mixture is less intense than that of the separate components.
- 'Diluent'
  Substance that serves primarily to reduce the concentration of the other ingredients in a formulation; volatile liquid that is added to modify the consistency or other properties. The term is most often used for liquid formulations, with the term filler used for solid or powder formulations.
- 'Dispersing agent'
  Substance added to a suspending medium or suspension to improve the separation of particles; to ensure proper dispersion; to prevent settling or clumping; to encourage uniform and maximum separation of individual, extremely fine solid particles or liquid droplets, often of colloidal size. A typical use is dispersal of dyes to ensure uniform coloration.
- 'Drier'
  These substances, which speed the drying of paint, ink, etc., are often organometallic compounds.
- 'Durability agent'
  Durability agents are ingredients added to increase the durability and therefore the functional life of a material.
- 'Dust suppressant'
  Substance used to control finely grained solid particles to reduce their discharge into the air.
- 'Dusting agent'
  Substance that is dusted onto the surface of a material (e.g., rubber) to reduce surface tack.
- 'Dye'
  Substance used to impart colour to other materials or mixtures; added to a material to add colour; soluble. Molecularly dispersed within a liquid, transferred to a material, and bound to that material through intermolecular forces. Typically an organic substance, although exceptions do exist. A dye requires some degree of solubility that allows it diffuse into the polymeric matrix of a textile fibre.
- 'Elasticizer'
  Substance that increases the elasticity of a material.
- 'Embalming agent'
  Substance used for the preservation of biological tissue.
- 'Energy releasers (explosives, motive propellant)'
  Substance characterized by chemical stability, but may be induced to undergo rapid chemical change without an outside source of oxygen, rapidly producing a large quantity of energy and gas accompanied by a large increase in volume and an explosion, bursting, or expansion.
- 'Etching agent'
  Etching Agent is a substance that removes unprotected areas of metal or glass surfaces. Etching agents are usually acids or bases.
- 'Explosion inhibitor'
  Substance used to reduce the explosion potential of flammable materials.
- 'Fertilizers (soil amendments)'
  Chemical substance used to increase the productivity and quality of farm crops, including plants, animals, and forestry; added to soil to supply chemical elements needed for plant nutrition.
- 'Filler'
  Ingredient added to fill out a dry product formulation and to lower the concentration of other ingredients; used to provide bulk, increase strength, increase hardness, or improve resistance to impact; used to extend a material and to reduce its cost by minimizing the amount of more expensive substances used in the production of articles; used to fill cavities or tighten joints; relatively inert and normally non-fibrous, finely divided substance added usually to extend volume and sometimes to improve desired properties, such as whiteness, consistency, lubricity, density or tensile strength.
- 'Film former'
  Any component of a material that aids the material in forming a thin continuous sheet on its substrate. This sheet will act as a barrier between the environment and its substrate. Silicone is a good filmformer in furniture polishes because of its ease of application, soil removal, and depth of glossiness. Polymers are the most commonly used film formers.
- 'Finishing agents'
  Chemical substances used to impart such functions as softening, staticproofing, wrinkle resistance, and water repellence. Substances may be applied to textiles, paper, and leather.
- 'Fire extinguishing agent'
  Any agent incorporated or applied to slow down combustion once started; Removes heat faster than it is released; separates the fuel and oxidizing agent; dilutes the vapour phase concentration of the fuel and oxidizing agent below what is needed for combustion.
- 'Fixing agent (mordant)'
  Substance used to interact with a dye on fibres to improve fastness.
- 'Flame retardant'
  Flame retardation is a process by which the normal degradation or combustion processes of polymers have been altered by the addition of certain chemicals. They are substances used on the surface of or incorporated into combustible materials to reduce or eliminate their tendency to ignite when exposed to heat or a flame for a short period of time; used to raise its ignition point; used to slow down or prevent combustion.
- 'Flocculating agent'
  A flocculating agent is a chemical or substance that facilitates flocculation of suspended solids in liquid. Flocculating agents are chemical additives, which, at relatively low levels compared to the weight of the solid phase, increase the degree of flocculation of a suspension. They act on a molecular level on the surfaces of the particles to reduce repulsive forces and increase attractive forces. The principal use of flocculating agents is to aid in making solid–liquid separations.
- 'Flotation agent'
  Substance used to concentrate and obtain minerals from ores.
- 'Flow promoter'
  Substance that reduces drag in fluids in motion and between a fluid and a conduit surface.
- 'Flux agent'
  Substance used to promote the fusing of minerals or prevent oxide formation; for casting or joining materials.
- 'Foamant'
  Any substance that promotes or enhances formation of a lather or foam (i.e., a dispersion of a gas in a liquid or solid); used to form physically, by expansion of compressed gases or vaporization of liquid, or chemically, by decomposition evolving a gas, a foam or cellular structure in a plastic or rubber material.
- 'Food flavouring and nutrient'
  Substance used in food or animal feedstuffs to produce or enhance taste or odour or nutritional value. Flavour compounds are molecules that stimulate the human taste chemical senses.

- 'Fragrance'
  Chemical substances used to impart control odours or impart pleasing odours. Fragrance compounds are molecules that stimulate the human olfactory chemical senses.
- 'Freeze-thaw additive'
  These synthetic resin emulsions or synthetic lattices enable paints, coatings, and other products to retain original consistency and to resist coagulation when exposed to freezing and thawing prior to application.
- 'Friction agent'
  Materials used to enhance friction between two objects.
- 'Fuel'
  Chemical substance used to create mechanical or thermal energy through chemical reactions; used to evolve energy in a controlled combustion reaction.
- 'Fuel additive'
  Substances added to a fuel for the purpose of controlling the rate of reaction or limiting the production of undesirable combustion products; provide other benefits such as corrosion inhibition, lubrication, or detergency.
- 'Gelling modifier'
  Substance that influences the formation or destruction of a gel.
- 'Hardener'
  Increases the strength, hardness, and abrasion resistance of coatings, adhesives, sealants, elastomers, and other products.
- 'Heat stabilizer'
  Substance that protect polymers from the chemical degrading effects of heat or UV irradiation.
- 'Heat transferring agent '
  Substance used to transmit or to remove heat from another material.
- 'Humectant'
  Humectant is a substance that is used to retard moisture loss from the product during use. This function is generally performed by hygroscopic materials. The efficacy of humectants depends to a large extent on the ambient relative humidity.
- 'Hydraulic (functional) fluids '
  Liquid or gaseous chemical substances used for transmitting pressure and EP-additives. Transfer power in hydraulic machinery.
- 'Impregnation agent'
  Substance used to admix with solid materials, which retain their original form.
- 'Incandescent agent'
  Substance that is used to emit electromagnetic radiation at high temperature.
- 'Insulators'
  Substances used to prevent or inhibit the flow of heat, electrical current, light, and the transmission of sound between two media. (acoustic, electrical, and thermal insulators).
- 'Intermediate (precursor)'
  Chemical substances consumed in a reaction in order to manufacture other chemical substances at an industrial processing facility.
- 'Ion exchange agent'
  Chemical substances, usually in the form of a solid matrix, that are used to selectively remove targeted ions from a solution. In ion exchange, ions of a given charge (either cations or anions) in a solution are adsorbed on a solid material (the ion exchanger) and are replaced by equivalent quantities of other ions of the same charge released by the solid.
- 'Leaching agent'
  Substance that, when added to a solvent, aids in the dissolution of a component of an insoluble solid mixture.
- 'Lubricating agent'
  Substance introduced between two moving surfaces or adjacent solid surface to reduce the friction between them, improve efficiency, reduce wear, and reduce heat generation; enhance the lubricity of other substances. These lubricating films are designed to minimize contact between the rubbing surfaces and to shear easily so that the frictional force opposing the rubbing motion is low.
- 'Luminescent agent'
  Substance that emits visible radiation upon absorption of energy in the form of photons, charged particles, or chemical change.
- 'Magnetic element'
  Substance added into materials in order to make them magnetic.
- 'Monomers'
  tance usually containing carbon and of a low molecular weight and simple structure which is capable of conversion to polymers, synthetic resins, or elastomers by repetitive combination with itself or other similar molecules.
- 'No technical function'
  To be used in the cases where the substance does not fulfil any particular technical function during the use described (e.g. case where a processing aid remains in the matrix of an article without fulfilling any technical function during service life)
- 'Opacifier'
  Substance that renders solutions opaque; reduces transparency or the ability of light to pass through solution; added to finished products to reduce their clear or transparent appearance.
- 'Oxidizing agent'
  Oxidizing agent is a substance that gains electrons during their reaction with a reducing agent. Oxidizing agents commonly contribute oxygen to other substances.
- 'pH regulating agent'
  Maintains the desired pH range of a substance; used to alter, stabilize, or control the pH (hydrogen ion concentration). Substances used to alter or stabilize the hydrogen ion concentration (pH).
- 'Photochemical'
  Chemical substance used for its ability to alter its physical or chemical structure through absorption of light, resulting in the emission of light, dissociation, discoloration, or other chemical reaction; used to create a permanent photographic image.
- 'Pigment'
  Any substance, usually in the form of a dry powder, that imparts colour to another substance or mixture by attaching themselves to the surface of the substrate through binding or adhesion; may contribute towards opacity, durability, and corrosion resistance. Must have positive colorant value; larger than molecular particle size and held in place by corresponding low mobility; scatter and absorb light.

  Pigments differ from dyes in that they are insoluble in the vehicle and exist as dispersed compounds in paint rather than as a solute.
- 'Plasticizer'
  An organic compound that softens synthetic polymers; added to a high polymer to facilitate processing and to increase flexibility, plasticity, fluidity and toughness of the final product by internal modification (solution) of the polymer molecule. Plasticizers may be added internally or externally. A rigid polymer can also be externally plasticized by addition of a plasticizer, which imparts the desired flexibility but is not chemically changed by reaction with the polymer.
- 'Plating agent'
  Substances/materials used as a source for a layer of metal deposited on another surface, or that aid in such a deposition. These are used in processes such as electroplating, galvanization or coating.

- 'Pressure transfer agent'
  Lubricating oil and grease additive that prevents metal to metal contact at high temperatures or under heavy loads where severe sliding conditions exist. Functions by reacting with the sliding metal surfaces to form oil-insoluble surface films.
- 'Process regulator'
  Chemical substance used to change the rate of a chemical reaction, start or stop the reaction, or otherwise influence the course of the reaction. May be consumed or become part of the reaction product.
- 'Processing aid'
  Chemical substances used to improve the processing characteristics or the operation of process equipment or to alter or buffer the pH of the substance or mixture, when added to a process or to a substance or mixture to be processed. Processing agents do not become a part of the reaction product and are not intended to affect the function of a substance or article created.
- 'Propellants, nonmotive (blowing agents)'
  Substance that is used for expelling products from pressurized containers (aerosol products); used to dissolve or suspend other substances and either to expel those substances from a container in the form of an aerosol or to impart a cellular structure to plastics, rubber, or thermo set resins; provides the force necessary to expel the contents of aerosol containers; liquefied or compressed gas within which substances are dissolved or suspended and expelled from a container upon discharge of the internal pressure through expansion of the gas. The formulated product in the pressurized container may be solution, emulsion, or suspension.
- 'Reactive cleaning/removal agent'
  Substance that reacts with and removes surface contaminants and is generally consumed, e.g., oxides, sulfides.
- 'Reducing agent'
  Substance that during reactions with oxidizing agents lose electrons; commonly contributes hydrogen to other substances; used to remove oxygen, hydrogenate or, in general, acts as electron donor in chemical reactions.
- 'Refrigerants'
  Substances used within machines such as air conditioning units, refrigerators, and walk in freezers to cool indoor air and reduce temperatures.
- 'Resins (prepolymers)'
  Usually high molecular weight polymers that lower viscosity. Thermoplastic resins soften when exposed to heat and return to original form at room temperature, and thermosetting resins solidify irreversibly when heated due to cross-linking.
- 'Semiconductor and photovoltaic agent'
  Substance that has resistivity between that of insulators and metals; usually changeable by light, heat or electrical or magnetic field; generates electromotive force upon the incidence of radiant energy.
- 'Sizing agent'
  Substance applied to substrates such as fabric, yarn, paper products, or plaster to increase abrasive resistance, stiffness, strength, smoothness, or reduce absorption.
- 'Softener'
  Substance used for softening materials to improve feel, to facilitate finishing process, or to impart flexibility or workability; used in textile finishing to impart superior ”hand” to the fabric and facilitate mechanical processing; has the capability of imparting softness and pliability to washable textile fabrics.
- 'Solids separation (precipitating) agent'
  Chemical substances used to promote the separation of suspended solids from a liquid.
- 'Solubility enhancer'
  A chemical additive that prevents chemicals or materials from separating or falling out of solution. Solubility enhancers are often used in concentrated formulations.
- 'Solvent'
  Any substance that can dissolve another substance (solute) to form a uniformly dispersed mixture (solution) at the molecular or ionic size level; provides dissolving capability required for a stable formulation; dissolves certain components of the formulation to aid dispersion of components; aids oil cleansing power and controls film drying rate; allows the product to solubilize soils on surfaces and facilitate removal; used to dissolve, thin, dilute, and extract.
- 'Stabilizing agent'
  A substance that tends to keep a compound, solution, or mixture from changing its form or chemical nature; renders or maintains a solution, mixture, suspension, or state resistant to chemical change; used to prevent or slow down spontaneous changes in and ageing of materials.
- 'Surface modifier'
  Substance that may be added to other ingredients to adjust the optical properties associated with the surface of a material. These substances are designed to affect the luster, increase gloss, and alter the reflectance exhibited by a surface.
- 'Surfactant'
  A surface active agent (surfactant) which, when added to water, causes it to penetrate more easily into, or to spread over the surface of another material by reducing the surface tension of the water (see detergent).
- 'Swelling agent'
  Substance added to a material to cause that material to increase in volume and become softer.
- 'Tackifier'
  Provides stickiness
- 'Tanning agent'
  Substance used for treating hides and skins.
- 'Terminator/Blocker'
  Substance that reacts with the end of a growing polymer chain, stopping further polymerization (terminator) or a substance used to protect a reactive moiety on a precursor during organic synthesis of a product that is subsequently removed regenerating the reactive moiety (blocker).
- 'Thickener/Thickening agent'
  Any of a variety of hydrophilic substances used to increase the viscosity of liquid mixtures and solutions and to aid in maintaining stability by their emulsifying properties. Four classifications are recognized: 1) Starches, gums, casein, gelatin and phycocolloids; 2) semisynthetic cellulose derivatives (e.g. carboxymethyl-cellulose); 3) polyvinyl alcohol and carboxy-vinylates (synthetic); and 4) bentonite, silicates, and colloidal silica.
- 'Tracer'
  Substance that possesses a readily detectable radioactive/isotopic label or chemical moiety which is added to biological/environmental media or chemical reactions to elucidate the transformation/transportation processes that are occurring.
- 'UV stabilizer'
  Substance that protects the product from chemical or physical deterioration induced by ultraviolet light; absorbs UV radiation, thereby protecting varnishes and pigments against UV degradation.
- 'Vapour pressure modifiers'
  Substance added to a liquid to modify its vapour pressure (e.g., to reduce evaporation).
- 'Vehicle (carrier)'
  The vehicle dissolves or disperses solid components of a substance, allowing even dispersion throughout application. The vehicle carries the other particles within a substance.
- 'Viscosity modifier'
  Substance used to alter the viscosity of another substance; used to decrease or increase the viscosity of finished products; used to modify the flow characteristics of other substances, or mixtures, to which they are added; controls the deformation or flow ability of a wax product. Resins generally lower viscosity while thickeners (e.g., gums and hydroxyethyl cellulose) increase viscosity.
- 'Waterproofing agent'
  A water repellent material functions by lowering the surface energy to protect surfaces against water by making water bead.
- 'X-Ray Absorber'
  Substance use to block or attenuate X-rays.

- 'Other'

9.2 Defined collections

ERCs defines a sequence containing ERC enumerates.
LCSs defines a sequence containing LCS enumerates.
PROCs defines a sequence containing PROC enumerates.
SUs defines a sequence containing SU enumerates.
PCs defines a sequence containing PC enumerates.
ACs defines a sequence containing AC enumerates.

Operators

function ECHA_USE_KB::ERC_Domain(lcs :: LCS):: ERCs

C1	lcs	LCS_M	LCS_F	LCS_IS	LCS_PW	LCS_C	LCS_SL	ELSE
A1	result := ERC→Enumerates							X
A2	result := ERCs{ERC1}	X						
A3	result := ERCs{ERC2, ERC3}		X					
A4	result := ERCs{ERC4, ERC6b, ERC6a, ERC6c, ERC6d, ERC5, ERC7}			X				
A5	result := ERCs{ERC8a, ERC8d, ERC8b, ERC8e, ERC8c, ERC8f, ERC9a, ERC9b}				X	X		
A6	result := ERCs{ERC10a, ERC11a, ERC10b, ERC11b, ERC12a, ERC12b, ERC12c}						X	
		R1	R2	R3	R4	R5	R6	R7

function ECHA_USE_KB::LCS_Domain(erc :: ERC):: LCSs

C1	erc	nil	ELSE					
C2	erc	-	ERC1	ERC2, ERC3	ERC4, ERC6b, ERC6a, ERC6c, ERC6d, ERC5, ERC7	ERC8a, ERC8d, ERC8b, ERC8e, ERC8c, ERC8f, ERC9a, ERC9b	ERC10a, ERC11a, ERC10b, ERC11b, ERC12a, ERC12b, ERC12c	ELSE
A1	result := LCS→Enumerates	X						X
A2	result→Add(#)		LCS_M	LCS_F	LCS_IS	LCS_PW	LCS_SL	
A3	result→Add(#)					LCS_C		
		R1	R2	R3	R4	R5	R6	R7

Chapter 10 ACTIVITY_KB

10.1 Defined enumerations

AC_SYNTHESIS

- 'flame pyrolysis'
  In gas-phase processes: nanoparticles are produced by using the heat to initiate the chemical reactions.
- 'mechanical synthesis'
  In contrast to other synthesis groups where nanoparticles were built "bottom-up" from individual molecules, in mechanical reduction nanoparticles are produced top down from larger particles.
- 'wet chemistry'
  Examples of wet chemistry within a solution are sol gels and the production of Ag by silver nitrate reduction. Synthesis into a solution is more related to the harvesting of nanosilver.
- 'chemical vapor condensation'
  In gas-phase processes nanoparticles are produced by using the heat to initiate the chemical reactions.
- 'laser ablation'
  Laser ablation is the process of removing material from a solid (or occasionally liquid) surface by irradiating it with a laser beam
- 'reactive sintering'
  Sintering is the process of compacting and forming a solid mass of material by heat and/or pressure without melting it to the point of liquefaction.

AC_IMPACTION_DRY_CONTAMINATED_OBJECTS

Activities where impaction or striking of a tool on an object contaminated with powder or granules potentially results in re-suspension of that powder (e.g. hammering, punching). For this activity class, exposure is estimated to be related to the level of contamination on the surface or the object that is impacted on.

- 'hammering'
- 'nailing'
- 'piling'
- 'punching'
- 'gouging'
- 'tuck pointing'

AC_HANDLING_DRY_CONTAMINATED_OBJECTS

Handling or transport of surfaces, objects, or pastes that are (potentially) contaminated with powders or granules (e.g. sorting, stacking, plastering). For this activity class, exposure is estimated to the contamination on the surface, object, or paste.

- 'sorting'
- 'stacking'
- 'carrying'
- 'picking / collecting objects'
- 'packaging'
- 'paving'
- 'wrapping'
- 'disposal of empty bags'
- 'plastering'
- 'kneading'
- 'modelling of product'
- 'bending metal tubes'

AC_MOVEMENT_AGITATION_POWDERS_GRANULES

Activities where movement and agitation of powders results in disturbances of the product causing dust particles to become airborne (e.g. sweeping, mixing, sieving).

- 'sweeping'
- 'application of compressed air'
- 'vacuum cleaning'
- 'mixing'
- 'weighing'
- 'raking'
- 'sieving'
- 'formulation into a solid mixture'
- 'wiping'

AC_FALLING_POWDERS_GRANULES

Activities where a stream of powder is transferred from one reservoir (or container, vessel) to the receiving vessel. The product may either fall due to gravity from a high to a lower point (e.g. dumping of powders), be transferred horizontally (e.g. scooping of powders).

- 'bagging solids'
- 'dumping solids in mixers (formulation)'
- 'loading barges with minerals or cereals'
- 'scooping'
- 'scattering'
- 'filling of bottles (powder)'

AC_VACUUM_TRANSFER_POWDERS_GRANULES

Activities where a stream of powder is transferred from one reservoir (or container, vessel) to the receiving vessel. Transfer through a hose or tube with pressure (e.g. vacuum transfer).

- 'vacuum transfer'

AC_COMPRESSING_POWDERS_GRANULES

Activities where powders, granules, or pelletized material are compressed due to compaction or crushing (e.g. tabletting, rolling).

- '(steam) rolling'
- 'compacting'
- 'tabletting'
- 'granulation'
- 'pelletization'
- 'pressing'

AC_FRACTURING_POWDERS_GRANULES

Activities where powders, granules, or pelletized material are crushed and broken into smaller parts or sizes due to frictional forces (between two surfaces or objects; e.g. grinding minerals)

- 'grinding minerals'
- 'milling cereals'
- 'very small scale crushing'
- 'testing tablets'
- 'de-lumping (breaking up product)'
- 'large scale bulk milling'

AC_SPRAY_APPLICATION_POWDERS

Spraying activities used to intentionally disperse powders on surfaces by using a pressure difference (e.g. dusting crops, powder coating).

- 'dusting crops'
- 'powder coating'
- 'spraying of concrete'

AC_SURFACE_SPRAYING_LIQUIDS

Activities used to atomize liquids into droplets for dispersion on surfaces (surface spraying; e.g. paint spraying, pest control operations).Spraying techniques may be used for dispersion of e.g. pesticides,biocides, and paints.

- 'spray application of paints on e.g. ships (using hvlp or airless techniques)'
- 'spray application of paints by spray can'
- 'spray application of paints by pneumatic spraying'
- 'pest control operations (using backpack)'
- 'spraying cleaning agents onto surfaces'
- 'foaming'
- 'tractor mounted spraying'
- 'application of dispersions containing NMs onto surfaces by spraying (outdoors)'
- 'spraying of dispersions containing NMs onto surfaces (indoor)'

AC_SPRAYING_LIQUIDS_IN_SPACE

Activities used to atomize liquids into droplets for dispersion into air (space spraying; e.g. fogging, fly spray). Spraying techniques may be used for dispersion of e.g. pesticides, biocides, and paints.

- 'spraying room deodorizers or fragrances'
- 'fogging'
- 'fly spray'

AC_ACTIVITY_UNDISTURBED_LIQUID_SURFACE

Handling of a liquid product in a bath or other reservoir. The liquid is relatively undisturbed (e.g. manual stirring, dipping in bath).

- 'dipping objects in a cleaning bath (where presence of treated surfaces in the area is limited)'
- 'dip-bad dry method, exhaustion'
- 'road coating'
- 'immersion of objects'
- 'manual stirring of paint'
- 'mixing and loading liquid cleaning products or desinfectants (e.g. laundry products, diluting, dissolving tablets)'
- 'tank dipping'
- 'bleaching'
- 'machining'
- 'wiping (liquids)'
- 'cleaning a surface with liquid or desinfectant (e.g. all-purpose cleaners, toilet cleaners)'
- 'waving'

AC_ACTIVITY_AGITATED_LIQUID_SURFACE

Handling of a liquid product in a bath or other reservoir. The liquid is agitated (e.g. gas bubbling, mechanical mixing in vessel, electroplating).

- 'electroplating'
- 'bath with gas bubbling'
- 'mechanical mixing/blending of paint'
- 'aeration of waste water'
- 'boiling'
- 'shaking liquids (e.g. in chemical laboratories)'
- 'grinding (in liquid)'
- 'formulation into a mixture'

AC_SPREADING_OF_LIQUIDS

Activities where liquid products are spread onto a surface (e.g. painting a ceiling/wall with roller or brush, laminating).

- 'painting with roller and brush'
- 'pouring a liquid flooring material on a floor'
- 'cleaning of liquid spills'
- 'gluing'
- 'mopping'
- 'embalming'
- 'laminating'
- 'lubricating'
- 'sponging'
- 'screen printing'
- 'cleaning of oil residue from bulk tanks'

AC_APPLICATION_LIQUIDS_HIGH_SPEED_PROCESSES

High energy activities with e.g. rotating tools where liquids are added to the process (e.g. metal working fluids).

- 'use of metal working fluids with e.g. circular saws and drills'
- 'centrifuging wet items'
- 'press printing'

AC_FALLING_LIQUIDS

Activities where a stream of liquid product is transferred from one reservoir to the next. The stream falls or glide from high to a lower point (falling liquids; e.g. filling of drums, tanker top loading) or is transferred with pressure (pressurized transfer: e.g. bottom loading).

- 'top loading of tanker at bulk terminal (boats, rail car or truck)'
- 'filling of drums'
- 'pouring'
- 'filling of bottles (liquid)'
- 'filling of paintgun'
- 'refueling of cars'
- 'manual calibration of fuel pump'
- 'over wing refueling of aircraft'
- 'arterial flushing / manual injection'
- 'sprinkling'

AC_BOTTOM_LOADING_LIQUIDS

Activities where a stream of liquid product is transferred from one reservoir to the next. The stream is transferred with pressure (pressurized transfer: e.g. bottom loading).

- 'bottom loading of tankers at bulk terminal'
- 'under wing refueling of aircraft'
- 'transfer of additives in tanker using bottom loading'

AC_HANDLING_LIQUID_CONTAMINATED_OBJECTS

Handling of solid objects that are treated or contaminated with the liquid of interest (e.g. handling of contaminated tools, evaporation from painted surface).

- 'handling of contaminated tools'
- 'evaporation from surface'

AC_FRACTURING_ABRASION_SOLID_OBJECTS

Activities where solid objects are broken into smaller parts or are abraded due to frictional forces (e.g. crushing, sawing, sanding)

- 'soldering'
- 'crushing concrete'
- 'jack hammering'
- 'pulverizing'
- 'sawing using a circular saw'
- 'milling (manually)'
- 'sanding'
- '(Cut-off) grinding of steel'
- 'drilling'
- 'buffing'
- 'polishing'
- 'chiseling'
- 'cutting'
- 'logging'
- 'demolishing with wrecking ball'
- 'wrecking'
- 'shredding'
- 'wire drawing'
- 'cold rolling of metal sheets'
- 'scraping'
- 'woodworking'

AC_ABRASIVE_BLASTING

A surface preparation technique for removing coatings or contamination by propelling abrasive material towards the surface at high velocity (e.g. grit blasting).

- 'grit blasting'
- '(ultra) High pressure (sand)blasting for stripping paint'
- 'water cutting'
- 'welding'

AC_CONSUMER_ARTICLE_USAGE
- 'wearing textiles'
- 'washing textiles'
- 'using food contact materials'
- 'use of articles with low release (outdoor)'
- 'use of articles with high or intended release (outdoor)'
- 'use of articles with low release (indoor)'
- 'use of articles with high release (indoor)'
- 'use of articles with no release of NM (closed systems, e.g. batteries, or diesel filter inside cars)'
- 'use of textiles (washing + wearing)'
- 'use of children´s toys'

AC_CONSUMER_PRODUCT_USAGE
- 'apply cosmetic directly on skin'
- 'apply cosmetic by spraying'
- 'use of cosmetics'
- 'use of antifouling paints (aquatic)'
- 'use of paints (outdoor walls)'
- 'use of packaging materials'
- 'use of pest control products'

AC_WEATHERING
- 'degradation of solid objects due to weathering'

AC_BURNING_OF_LIQUIDS

AC_BURNING_OF_SOLIDS

AC_HARDENING_MELTING_PROCESSES

AC_HOT_SOLID_HANDLING

AC_HOT_LIQUID_HANDLING

AC_EXTRUDING

ActivityClass
- 'use at industrial site leading to inclusion into/onto article'
- 'fabric manufacturing by dip-pad dry / exhaustion processes'
- 'cosmetic manufacturing process, formulation into solid matrix'
- 'polymeric nanocomposites manufacturing by extrusion / compounding'
- 'cosmetic manufacturing process, formulation into a liquid mixture'
- 'use of polymeric nanocomposites (outdoors)'
- 'use of photocatalytic coatings on roads (outdoors)'
- 'incineration'
  Activities where a solid/liquid product is incinerated in a waste incineration plant.

Operators

function ACTIVITY_KB::Potential_AC_Categories (ca : ContributingActivity) :: Enumerations

C1	ca.use.used_material_appearance	maSolidObject				maFirmGranulates				maPowder				maLiquid				maGas				ELSE
C2	ca.ca_perspective	occupa-tional	con-sumer	envir-on-mental	ELSE	occupa-tional	con-sumer	envir-on-mental	ELSE	occupa-tional	con-sumer	envir-on-mental	ELSE	occupa-tional	con-sumer	environ-mental	ELSE	occupa-tional	con-sumer	environ-mental	ELSE	-
A1	result→Add(AC_SYNTHESIS)																					
A2	result→Add(AC_IMPACTION_DRY_CONTAMINATED_OBJECTS)	X																				
A3	result→Add(AC_HANDLING_DRY_CONTAMINATED_OBJECTS)	X																				
A4	result→Add(AC_MOVEMENT_AGITATION_POWDERS_GRANULES)					X				X												
A5	result→Add(AC_FALLING_POWDERS_GRANULES)					X				X												
A6	result→Add(AC_VACUUM_TRANSFER_POWDERS_GRANULES)					X				X												
A7	result→Add(AC_COMPRESSING_POWDERS_GRANULES)					X				X												
A8	result→Add(AC_FRACTURING_POWDERS_GRANULES)					X				X												
A9	result→Add(AC_SPRAY_APPLICATION_POWDERS)									X												
A10	result→Add(AC_SURFACE_SPRAYING_LIQUIDS)													X								
A11	result→Add(AC_SPRAYING_LIQUIDS_IN_SPACE)													X								
A12	result→Add(AC_ACTIVITY_UNDISTURBED_LIQUID_SURFACE)													X								
A13	result→Add(AC_ACTIVITY_AGITATED_LIQUID_SURFACE)													X								
A14	result→Add(AC_SPREADING_OF_LIQUIDS)													X								
A15	result→Add(AC_APPLICATION_LIQUIDS_HIGH_SPEED_PROCESSES)													X								
A16	result→Add(AC_FALLING_LIQUIDS)													X								
A17	result→Add(AC_BOTTOM_LOADING_LIQUIDS)													X								
A18	result→Add(AC_HANDLING_LIQUID_CONTAMINATED_OBJECTS)													X								
A19	result→Add(AC_FRACTURING_ABRASION_SOLID_OBJECTS)	X																				
A20	result→Add(AC_ABRASIVE_BLASTING)																					
A21	result→Add(AC_CONSUMER_ARTICLE_USAGE)		X																			
A22	result→Add(AC_CONSUMER_PRODUCT_USAGE)										X				X				X			
A23	result→Add(AC_WEATHERING)			X																		
A24	result→Add(AC_BURNING_OF_LIQUIDS)													X								
A25	result→Add(AC_BURNING_OF_SOLIDS)	X																				
A26	result→Add(AC_HARDENING_MELTING_PROCESSES)																					
A27	result→Add(AC_HOT_SOLID_HANDLING)	X																				
A28	result→Add(AC_HOT_LIQUID_HANDLING)													X								
A29	result→Add(AC_EXTRUDING)																					
		R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15	R16	R17	R18	R19	R20	R21

Chapter 11 SIMILARITY_KB

11.1 Defined enumerations

`CompareResult`
- `lower`
- `similar`
- `higher`

`SimType`
- `'n-fold'`
  The outcome of the similarity is based upon an n-fold difference.

`CompareStatus`
- `csNoRR`
- `csBelowRR`
- `csWithinRR`
- `csAboveRR`

`SimOutcome`
- `match`
- `nomatch`

11.2 Defined classes

Class `SimResult`

Attributes

name	type	domain	inference	comment
`score`	: `Real`			*Quantitative similarity result between two endpoint owners*
`outcome`	:: `any Enumerate`			*Qualitative outcome*
`sim_type`	:: `SimType`			*The type of similarity function applied.*
`status`	:: `CompareStatus`			

Operators

```
function SimResult.ColorStr(): String
  if outcome = match then
    result := "rgba(99,190,123,1)"
  else
    if outcome = nomatch then
      result := "rgba(248,105,107,1)"
    else
      if score ≤ 1.5 then
        result := "rgba(99,190,123,1)"
      else
        if score ≤ 5 then
          result := "rgba(255,235,132,1)"
        else
          result := "rgba(248,105,107,1)"
```

Operators

```
function SIMILARITY_KB::Similarity(epq : EP_Qualifier,dr : RelevanceObj,epo1 : EP_Owner,epo2 : EP_Owner ):: SimResult
  if epo1 = epo2 then
  begin
    result := SimResult→New;
    result.score := 1
  end
  else
  begin
    with epo1.DP_From(epq) | dp1 then
      with epo2.DP_From(epq) | dp2 then
        result := DP_Similarity(epq, dr, dp2, dp1)
  end

function SIMILARITY_KB::EP_Similarity(epq : EP_Qualifier,dr : RelevanceObj,epA : EP_Record,epB : EP_Record ):: SimResult
  with epA.dataobjects→Select(dp | dp.valid) | dpsA then
    with epB.dataobjects→Select(dp | dp.valid) | dpsB then
    begin
      if (dpsA→Size = 1) and (dpsB→Size = 1) then
      begin
        result := DP_Similarity(epq, dr, dpsB[1], dpsA[1])
      end
    end
```

```
function SIMILARITY_KB::DP_Similarity(epq : EP_Qualifier,dr : RelevanceObj,dpA : EP_DataObject,dpB : EP_DataObject ):: SimResult
  if dpA.data_type = dpB.data_type then
  begin
    /* TO DO VNR */  ;
    result := SimResult→New;
    if dr ≠ nil then
    begin
      if Known(dr.bio_relevance_max) and (dpA.value_y ≥ dr.bio_relevance_max) and (dpB.value_y ≥ dr.bio_relevance_max) then
      begin
        result.score := 1;
        result.status := csAboveRR;
        result.outcome := match
      end
      else
        if Known(dr.bio_relevance_min) and (dpA.value_y ≤ dr.bio_relevance_min) and (dpB.value_y ≤ dr.bio_relevance_min) then
        begin
          result.score := 1;
          result.status := csBelowRR;
          result.outcome := match
        end
        else
        begin
          result.score := dpA.value_y→Fold(dpB.value_y);
          if Known(dr.match_threshold) and (result.score ≤ dr.match_threshold) then
            result.outcome := match
          else
            if Known(dr.nomatch_threshold) and (result.score > dr.nomatch_threshold) then
              result.outcome := nomatch
        end
    end
    else
    begin
      case dpA.data_type of
        tTEXT:
          if dpA.text_y = dpB.text_y then
          begin
            result.score := 1;
            result.outcome := match
          end
          else
          begin
            result.score := 0;
            result.outcome := nomatch
          end;
        tENUM:
          if dpA.enum_y = dpB.enum_y then
          begin
            result.score := 1;
            result.outcome := match
          end
          else
          begin
            result.score := 0;
            result.outcome := nomatch
          end
        else
          begin
            result.score := dpA.value_y→Fold(dpB.value_y);
            result.status := csNoRR
          end
      end
    end
  end
```

```
function SIMILARITY_KB::CompositionSimilarity(mA :Material,mB :Material ):: SimResult
  with mA.core_chemistry | core_chemicals_A then
  begin
    with mB.core_chemistry | core_chemicals_B then
    begin
      result := ChemicalSimilarity(core_chemicals_A[1], core_chemicals_B[1])
    end
  end

function SIMILARITY_KB::SurfaceCompositionSimilarity(mA :Material,mB :Material ):: SimResult
  with mA.surface_chemistry | surface_chemicals_A then
  begin
    with mB.surface_chemistry | surface_chemicals_B then
    begin
      result := ChemicalSimilarity(surface_chemicals_A[1], surface_chemicals_B[1])
    end
    else
    begin
      result := SimResult→New;
      result.outcome := nomatch;
      result.score := 0
    end
  end
  else
    with mB.surface_chemistry | surface_chemicals_B then
    begin
      result := SimResult→New;
      result.outcome := nomatch;
      result.score := 0
    end
    else
    begin
      result := SimResult→New;
      result.outcome := match;
      result.score := 1
    end

function SIMILARITY_KB::ChemicalSimilarity(chA :Chemical,chB :Chemical ):: SimResult
  begin
    /* Same cas number = 1 */  ;
    with EPQ(PC_IDENTITY::ID_CAS_REG_NR) | epq_CAS_nr then
    begin
      with Similarity(epq_CAS_nr, nil, chA, chB) | sim_CAS then
      begin
        result := sim_CAS
      end
    end;
    if result = nil then
    begin
      /* Same ec number = 1 */    ;
      with EPQ(PC_IDENTITY::ID_EC_REG_NR) | epq_EC_nr then
      begin
        with Similarity(epq_EC_nr, nil, chA, chB) | sim_CAS then
        begin
          result := sim_CAS
        end
      end
    end;
    if (result ≠ nil) and (result.outcome = match) then
    begin
      /* Compare typical mass % */    ;
      with EPQ(PC_COMPOSITION::EP_MASS_CONC) | epq_mass_conc then
      begin
        with Similarity(epq_mass_conc, nil, chA, chB) | sim_mass_conc then
        begin
          result := sim_mass_conc
        end
      end
    end
  end
```

Chapter 12 GHS_KB

12.1 Defined enumerations

HCode

- H200
- H201
- H202
- H203
- H204
- H205
- H220
- H221
- H222
- H223
- H224
- H225
- H226
- H228
- H240
- H241
- H242
- H250
- H251
- H252
- H260
- H261
- H270
- H271
- H272
- H280
- H281
- H290
- H300
- H301
- H302
- H304
- H310
- H311
- H312
- H314
- H315
- H317
- H318
- H319
- H330
- H331
- H332
- H334
- H335
- H336
- H340
- H341
- H350
- H351
- H360
- H361
- H362
- H370
- H371
- H372
- H373

- H400
- H410
- H411
- H412
- H413
- H420
- EUH001
- EUH006
- EUH014
- EUH018
- EUH019
- EUH029
- EUH031
- EUH032
- EUH044
- EUH059
- EUH066
- EUH070
- EUH071
- EUH201
- EUH201A
- EUH202
- EUH203
- EUH204
- EUH205
- EUH206
- EUH207
- EUH208
- EUH209
- EUH209A
- EUH210
- EUH401

GHSxx

- GHS01
- GHS02
- GHS03
- GHS04
- GHS05
- GHS06
- GHS07
- GHS08
- GHS09

12.2 Defined classes

Class CLP_Hazard

Attributes

name	type	domain	inference	comment
hcode	:: HCode			
generic_concentration_limit	: percentage			*https://www.chemsafetypro.com/Topics/GHS/GHS_cut_off_value_GHS_concentration_limit.html*
specific_concentration_limit	: percentage	(# ≥ 0.0·%) and (# ≤ 100.0·%)		*"Specific Concentration Limit (SCL)"*

12.3 Defined collections

HCodes defines a sequence containing HCode enumerates.
GHScodes defines a sequence containing GHSxx enumerates.

Defined expressions

name	type	expression	comment
tox_phrases	: HCodes	HCodes{H300, H301, H302, H304, H310, H311, H312, H314, H315, H317, H318, H319, H330, H331, H332, H334, H335, H336, H340, H341, H350, H351, H360, H361, H362, H370, H371, H372, H373, H400, H410, H411, H412, H413, H420}	

Operators

```
function GHS_KB::HPhraseToStr( hp :: HCode ) :: String
  case hp of
    H200:
      result := "H200: Unstable explosives.";
    H201:
      result := "H201: Explosive; mass explosion hazard.";
    H202:
      result := "H202: Explosive, severe projection hazard.";
    H203:
      result := "H203: Explosive; fire, blast or projection hazard.";
    H204:
      result := "H204: Fire or projection hazard.";
    H205:
      result := "H205: May mass explode in fire.";
    H220:
      result := "H220: Extremely flammable gas.";
    H221:
      result := "H221: Flammable gas.";
    H222:
      result := "H222: Extremely flammable aerosol.";
    H223:
      result := "H223: Flammable aerosol.";
    H224:
      result := "H224: Extremely flammable liquid and vapour.";
    H225:
      result := "H225: Highly flammable liquid and vapour.";
    H226:
      result := "H226: Flammable liquid and vapour.";
    H228:
      result := "H228: Flammable solid.";
    H240:
      result := "H240: Heating may cause an explosion.";
    H241:
      result := "H241: Heating may cause a fire or explosion.";
    H242:
      result := "H242: Heating may cause a fire.";
    H250:
      result := "H250: Catches fire spontaneously if exposed to air.";
    H251:
      result := "H251: Self-heating: may catch fire.";
    H252:
      result := "H252: Self-heating in large quantities; may catch fire.";
    H260:
      result := "H260: In contact with water releases flammable gases which may ignite spontaneously.";
    H261:
      result := "H261: In contact with water releases flammable gases.";
    H270:
      result := "H270: May cause or intensify fire; oxidiser.";
    H271:
      result := "H271: May cause fire or explosion; strong oxidiser.";
    H272:
      result := "H272: May intensify fire; oxidiser.";
    H280:
      result := "H280: Contains gas under pressure; may explode if heated.";
    H281:
      result := "H281: Contains refrigerated gas; may cause cryogenic burns or injury.";
    H290:
      result := "H290: May be corrosive to metals.";
    H300:
      result := "H300: Fatal if swallowed.";
    H301:
      result := "H301: Toxic if swallowed.";
    H302:
      result := "H302: Harmful if swallowed.";
    H304:
      result := "H304: May be fatal if swallowed and enters airways.";
    H310:
      result := "H310: Fatal in contact with skin.";
    H311:
      result := "H311: Toxic in contact with skin.";
    H312:
      result := "H312: Harmful in contact with skin.";
    H314:
      result := "H314: Causes severe skin burns and eye damage.";
    H315:
      result := "H315: Causes skin irritation.";
```

```
H317:
  result := "H317: May cause an allergic skin reaction.";
H318:
  result := "H318: Causes serious eye damage.";
H319:
  result := "H319: Causes serious eye irritation.";
H330:
  result := "H330: Fatal if inhaled.";
H331:
  result := "H331: Toxic if inhaled.";
H332:
  result := "H332: Harmful if inhaled.";
H334:
  result := "H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled.";
H335:
  result := "H335: May cause respiratory irritation.";
H336:
  result := "H336: May cause drowsiness or dizziness.";
H340:
  result := "H340: May cause genetic defects.";
H341:
  result := "H341: Suspected of causing genetic defects.";
H350:
  result := "H350: May cause cancer.";
H351:
  result := "H351: Suspected of causing cancer.";
H360:
  result := "H360: May damage fertility or the unborn child.";
H361:
  result := "H361: Suspected of damaging fertility or the unborn child.";
H362:
  result := "H362: May cause harm to breast-fed children.";
H370:
  result := "H370: Causes damage to organs.";
H371:
  result := "H371: May cause damage to organs.";
H372:
  result := "H372: Causes damage to organs through prolonged or repeated exposure.";
H373:
  result := "H373: May cause damage to organs through prolonged or repeated exposure.";
H400:
  result := "H400: Very toxic to aquatic life.";
H410:
  result := "H410: Very toxic to aquatic life with long lasting effects.";
H411:
  result := "H411: Toxic to aquatic life with long lasting effects.";
H412:
  result := "H412: Harmful to aquatic life with long lasting effects.";
H413:
  result := "H413: May cause long lasting harmful effects to aquatic life.";
H420:
  result := "H420: Harms public health and the environment by destroying ozone in the uppper atmosphere";
EUH001:
  result := "EUH001: Explosive when dry.";
EUH006:
  result := "EUH006: Explosive with or without contact with air.";
EUH014:
  result := "EUH014: Reacts violently with water.";
EUH018:
  result := "EUH018: In use may form flammable/explosive vapour-air mixture.";
EUH019:
  result := "EUH019: May form explosive peroxides.";
EUH029:
  result := "EUH029: Contact with water liberates toxic gas.";
EUH031:
  result := "EUH031: Contact with acids liberates toxic gas.";
EUH032:
  result := "EUH032: Contact with acids liberates very toxic gas.";
EUH044:
  result := "EUH044: Risk of explosion if heated under confinement";
EUH059:
  result := "EUH059: Hazardous to the ozon layer.";
EUH066:
  result := "EUH066: Repeated exposure may cause skin dryness or cracking.";
EUH070:
  result := "EUH070: Toxic by eye contact.";
EUH071:
  result := "EUH071: Corrosive to the respiratory tract";
```

```
    EUH201:
      result := "EUH201: Contains lead. Should not be used on surfaces liable to be chewed or sucked by children.";
    EUH201A:
      result := "EUH201A: Warning! Contains lead.";
    EUH202:
      result := "EUH202: Cyanoacrylate. Danger. Bonds skin and eyes in seconds. Keep out of the reach of children.";
    EUH203:
      result := "EUH203: Contains chromium(VI). May produce an allergic reaction.";
    EUH204:
      result := "EUH204: Contains isocyanates. May produce an allergic reaction.";
    EUH205:
      result := "EUH205: Contains epoxy constituents. May produce an allergic reaction.";
    EUH206:
      result := "EUH206: Warning! Do not use together with other products. May release dangerous gases (chlorine).";
    EUH207:
      result := "EUH207: Warning! Contains cadmium. Dangerous fumes are formed during use. See information supplied by the manufacturer. Comply with the safety instructions.";
    EUH208:
      result := "EUH208: Contains <name of sensitising substance>. May produce an allergic reaction.";
    EUH209:
      result := "EUH209: Can become highly flammable in use. EUH209A: Can become flammable in use.";
    EUH210:
      result := "EUH210: Safety data sheet available on request.";
    EUH401:
      result := "EUH401: To avoid risks to human health and the environment, comply with the instructions for use."
    else
      result := "?"
  end


function GHS_KB::HPhraseToGHScode( hp :: HCode ) :: GHScodes
  case hp of
    H200, H201, H202, H203, H204, H240:
      result := GHScodes{GHS01};
    H220, H222, H223, H224, H225, H226, H228, H242, H250, H251, H252, H260, H261:
      result := GHScodes{GHS02};
    H241:
      result := GHScodes{GHS01, GHS02};
    H270, H271, H272:
      result := GHScodes{GHS03};
    H280, H281:
      result := GHScodes{GHS04};
    H290, H314, H318:
      result := GHScodes{GHS05};
    H300, H301, H310, H311, H330, H331:
      result := GHScodes{GHS06};
    H302, H312, H315, H317, H319, H332, H335, H336, H420:
      result := GHScodes{GHS07};
    H304, H334, H340, H341, H350, H351, H360, H361, H370, H371, H372, H373:
      result := GHScodes{GHS08};
    H400, H410, H411, H412, H413:
      result := GHScodes{GHS09}
  end
```

Chapter 13 TERMINOLOGY_KB

13.1 Defined enumerations

`Definitions`

General definitions and terminology not endpoint specific.

- `DEF_RELEASE`
  Release is the liberation of a nanomaterial (NM) during a natural or technical process at any given life cycle (LC) stage. Liberation may occur in three main release forms, i.e. air dispersed (aerosols), liquid dispersed (suspensions) and undispersed material, e.g. debris. It may be expressed without a specific metric, as a dispersion-specific fraction or percentage (to air-, liquid and undispersed) of the total release, or as a mass per unit area or unit quantity of the matrix. Release will be dependent on the physico-chemical properties of the NM and operational and environmental conditions. (D2.3-GRACIOUS)
- `DEF_EMISSION`
  Emission is the transfer of a liberated NM to a compartment and is usually expressed as a flow, e.g. quantity as mass or number of particles per unit time or unit of area, or particle per mass of product. Emission is often dependent on risk management measures (RMM) that are located at the source of a process, i.e. local controls that may alter the mass flow. Further along the substance flow, emission is dependent on the effectiveness of waste water treatment plants (WWTP) and solid waste incineration plants (MSWI). (D2.3-GRACIOUS)
- `DEF_EXPOSURE_SCENARIO`
  An exposure scenario refers to an identified use, or group of similar identified uses, such as formulation, processing or production of an article. It describes the operational conditions and risk management measures (RMM) thatensure safe use of the substance for that use.Exposure scenarios may include a number of "contributing scenarios". A contributing scenario describes each contributing activity within the identified use (e.g. mixing, pouring into small containers, applying asubstance by spraying etc.).
- `DEF_RISK_MANAGEMENT_MEASURE`
  The term "risk management measure" (RMM) means an activity or device that reduces or avoids the exposure of humans and the environment to a substance during its use. RMM applied in industrial uses include local exhaust ventilation (LEV), personal protective equipment (PPE), waste gas incinerators or onsite and municipal waste (water) treatment.
- `DEF_NF_EMISSION`
  The emission is the transfer of a released NF during a natural or technical process at any given life cycle stage (LCS) to a compartment. It is usually expressed as a flow rate (e.g. mass or number of particles per unit time or area, or per mass of product). Emission of NF depends mostly on the substance release potential (e.g. physico-chemical properties of the NF; characteristics of NEP matrix), the release mechanism (passive diffusion, dissolution, and desorption of the added NFs into liquid media; matrix degradation including photo-degradation, thermal decomposition, mechanical treatment, and hydrolysis), the specific activity or process (e.g. the type of energy involved), the environmental conditions during release as well as the level of material-aging.System dependant parameters such as risk management measures (RMM) which are located at the source of a process (e.g. presence of exposure controls in workplaces or presence of organic matter in soils) may reduce the emission of a substance and consequently reduce the likelihood of inhalation and/or dermal exposure. Further along the substance flow, emission and subsequent exposure is dependent on the effectiveness of waste water treatment plants (WWTP) and solid waste incineration plants (MSWI).

Chapter 14 CELL_KB

https://web.expasy.org/cellosaurus
https://www.proteinatlas.org/humanproteome/celltype
Primary cell : primary cells are isolated directly from tissues, have a finite lifespan and limited expansion capacity. Cells isolated directly from human or animal tissue
Cell line: Cells that have been continually passaged over a long period of time and have acquired homogenous genotypic and phenotypic characteristics. Cell lines can be finite or continuous. An immortalized or continuous cell line has acquired the ability to proliferate indefinitely, either through genetic mutations or artificial modifications. A finite cell line has been sub-cultured for 20-80 passages after which they senesce. Cell lines are preferably used for convenience as they are easy to handle and widely published. However, they are less preferred as a biologically relevant option, since they have lost the true characteristics of the original tissue from which they were isolated. Serial passaging is known to cause genotypic and phenotypic variation in cell lines. Variation can often be so far from that of the original tissue to where they do not mimic the in vivo environment very closely. Cells that do not represent the original tissue could result in false negative or false positive findings.
Cell culture: refers to the removal of cells from an animal or plant and their subsequent growth in a favorable artificial environment.

14.1 Defined enumerations

`CellModelDescriptor`

Used to identify a group/model of applicable cell types.

- `'2D culture model'`
- `'co-culture model'`
- `'3D culture model'`

`CellCoCultureDescriptors`

Used to identify a specific cell co-culture

- `'Calu-3 + MDM co-culture'`
- `'Calu-3 + dTHP-1 co-culture'`
- `'A549 + dTHP-1 co-culture'`

`CellLineDescriptor`

Descriptors for the different cell lines used in the assays.

- `'NR8383 (rat alveolar macrophages cell line)'`
  Rat alveolar macrophages cell line
- `'RAW 264.7 (mouse macrophages cell line)'`
- `'J774.A1 (mouse monocyte macrophage cell line)'`
- `'A549 (human alveolar cell line)'`
  Human
- `'Macrophages'`
  Does this represent different kinds of macrophages cell lines? If so, this one should be deleted and the more specific ones should be used instead.
- `'THP-1 (human leukemic monocyte cell line)'`
  human In general, THP-1 cells exhibit a large, round, single-cell morphology. The cells were derived from the peripheral blood of a 1-year-old human male with acute monocytic leukemia. (also ATCC TIB 202)
- `'MDM (human primary cells: monocyte-derived macrophages)'`
  Primary human cells
- `'dTHP-1'`
  differentiated THP-1 (dTHP-1) cells, human THP-1-derived macrophages (dTHP1)
- `'HEK293 (human embryonic kidney cell line)'`
  Human embryonic kidney 293 cells
- `'Calu-3 (human bronchial cell line)'`
  Calu-3 cells are a submucosal gland cell line, which was generated from a bronchial adenocarcinoma. Under air–liquid interface conditions Calu-3 cells grow in monolayers, producing mucus and cilia-like microvilli.
  Calu-3 is a human lung cancer cell line commonly used in cancer research and drug development. Calu-3 cells are epithelial and can act as respiratory models in preclinical applications.
- `'16HBE (human bronchial epithelial cell line)'`
  Immortalized 16HBE14o- Human Bronchial Epithelial Cell Lines
- `'EpiAlveolar (human 3D co-culture cell model)'`
  EpiAlveolar from supplier MatTek is a 3D co-culture model of the air-blood barrier. Produced from primary human alveolar epithelial cells, pulmonary endothelial cells and fibroblasts.
- `'MucilAir (human 3D cell model)'`
  MucilAir from supplier Epithelix is a 3D epithelium of the human upper respiratory tract made of primary low passage cells cultured at the air liquid interface.
- `'NRK-52E (rat, normal kidney cell line)'`
  Used in Protein carbonylation

- 'CACO-2 (human cell line)'
  Caco-2 is an immortalized cell line of human colorectal adenocarcinoma cells. It is primarily used as a model of the intestinal epithelial barrier.
- 'Caki-1 (human cell line)'
  Caki-1 is a human clear cell renal cell carcinoma (ccRCC) line that displays epithelial morphology and grows in adherent culture.
- 'HepG2 (human)'
  human hepatocarcinoma (HepG2) liver cells
- 'Hep3B (human)'
  human hepatoma (Hep3B) cells
- 'BEAS-2B (human lung epithelial cells)'
  Human lung epithelial BEAS-2B cells (BEAS-2B is also a human epithelial cell line which is commercially available and is an adenovirus-12 SV40 hybrid virus-transformed and non-tumorigenic cell line.)
- 'V79 (chinese hamster)'
  Chinese hamster lung fibroblast V79 cells
- 'TK6 (human lymphoblastoid cells)'
  TK6, human lymphoblastoid cell line
- '3T3 (mouse embryonic fibroblasts)'
  3T3 cells are several cell lines of mouse embryonic fibroblasts
- 'carp leukocyte cell line'
- 'Kupffer cells'
  Kupffer cells, also known as stellate macrophages and Kupffer–Browicz cells, are specialized cells localized in liver.
- 'HaCaT (human keratinocyte cells)'
  human keratinocyte HaCaT cell line

HCTG_EPITHELIAL_CELLS

- CT_ENTEROCYTES
- CT_MUCUS_SECRETING_CELLS
- CT_PANETH_CELLS
- CT_CILIATED_CELLS
- CT_CLUB_CELLS
- CT_EXOCRINE_GLANDULAR_CELLS
- CT_BASAL_GLANDULAR_CELLS
- CT_GLANDULAR_CELLS
- CT_BASAL_KERATINOCYTES
- CT_SUPRABASAL_KERATINOCYTES
- CT_CHOLANGIOCYTES
- CT_HEPATOCYTES
- CT_ALVEOLAR_CELLS_TYPE_1
- CT_ALVEOLAR_CELLS_TYPE_2
- CT_COLLECTING_DUCT_CELLS
- CT_DISTAL_TUBULAR_CELLS
- CT_PROXIMAL_TUBULAR_CELLS
- CT_DUCTAL_CELLS
- CT_SERTOLI_CELLS
- CT_UROTHELIAL_CELLS

HCTG_ENDOCRINE_CELLS

- CT_INTESTINAL_ENDOCRINE_CELLS
- CT_PANCREATIC_ENDOCRINE_CELLS
- CT_LEYDIG_CELLS

HCTG_NEURONAL_CELLS

- CT_CONE_PHOTORECEPTOR_CELLS
- CT_ROD_PHOTORECEPTOR_CELLS
- CT_BIPOLAR_CELLS
- CT_HORIZONTAL_CELLS

HCTG_GLIAL_CELLS

- CT_MULLER_GLIA_CELLS

HCTG_GEM_CELLS
- CT_SPERMATOGONIA
- CT_SPERMATOCYTES
- CT_EARLY_SPERMATIDS
- CT_LATE_SPERMATIDS

HCTG_TROPHOBLAST_CELLS
- CT_CYTOTROPHOBLASTS
- CT_SYNCYTIOTROPHOBLASTS
- CT_EXTRAVILLOUS_TROPHOBLASTS

HCTG_VASCULAR_CELLS
- CT_ENDOTHELIAL_CELLS

HCTG_MUSCLE_CELLS
- CT_CARDIOMYOCYTES
- CT_SMOOTH_MUSCLE_CELLS

HCTG_PIGMENT_CELLS
- CT_MELANOCYTES

HCTG_MESENCHYMAL_CELLS
- CT_FYBROBLASTS
- CT_LTO_CELLS
- CT_PERITUBULAR_CELLS

HCTG_UNDIFFERENTIATED_CELLS
- CT_UNDIFFERENTIATED_CELLS

HCTG_BLOOD_AND_IMMUNE_CELLS
- CT_B_CELLS
- CT_T_CELLS
- CT_GRANULOCYTES
- CT_MONOCYTES
- CT_MACROPHAGES
- CT_HOFBAUER_CELLS
- CT_KUPFFER_CELLS
- CT_ERYTHROID_CELLS

HTO

https://www.proteinatlas.org/humanproteome/tissue

- TO_EYE
- TO_RETINA
- TO_HEART
- TO_SKELETAL_MUSCLE
- TO_SMOOTH_MUSCLE
- TO_ADRENAL_GLAND
- TO_PARATHYROID_GLAND
- TO_THYROID_GLAND
- TO_PITUITARY_GLAND
- TO_LUNG
- TO_BONE_MARROW
- TO_LYMPHOID_TISSUE
- TO_LIVER
- TO_GALLBLADDER

- TO_TESTIS
- TO_EPIDIDYMIS
- TO_PROSTATE
- TO_SEMINAL_VESICLE
- TO_DUCTUS_DEFERENS
- TO_ADIPOSE_TISSUE
- TO_BRAIN
- TO_SALIVARY_GLAND
- TO_ESOPHAGUS
- TO_TONGUE
- TO_STOMACH
- TO_INTESTINE
- TO_PANCREAS
- TO_KIDNEY
- TO_URINARY_BLADDER
- TO_BREAST
- TO_VAGINA
- TO_CERVIX
- TO_ENDOMETRIUM
- TO_FALLOPIAN_TUBE
- TO_OVARY
- TO_PLACENTA
- TO_SKIN
- TO_BLOOD