HARMLESS

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 953183

HOUSEKEEPING RULES

Thank you for accepting these rules that shall ensure a smooth running of the workshop!

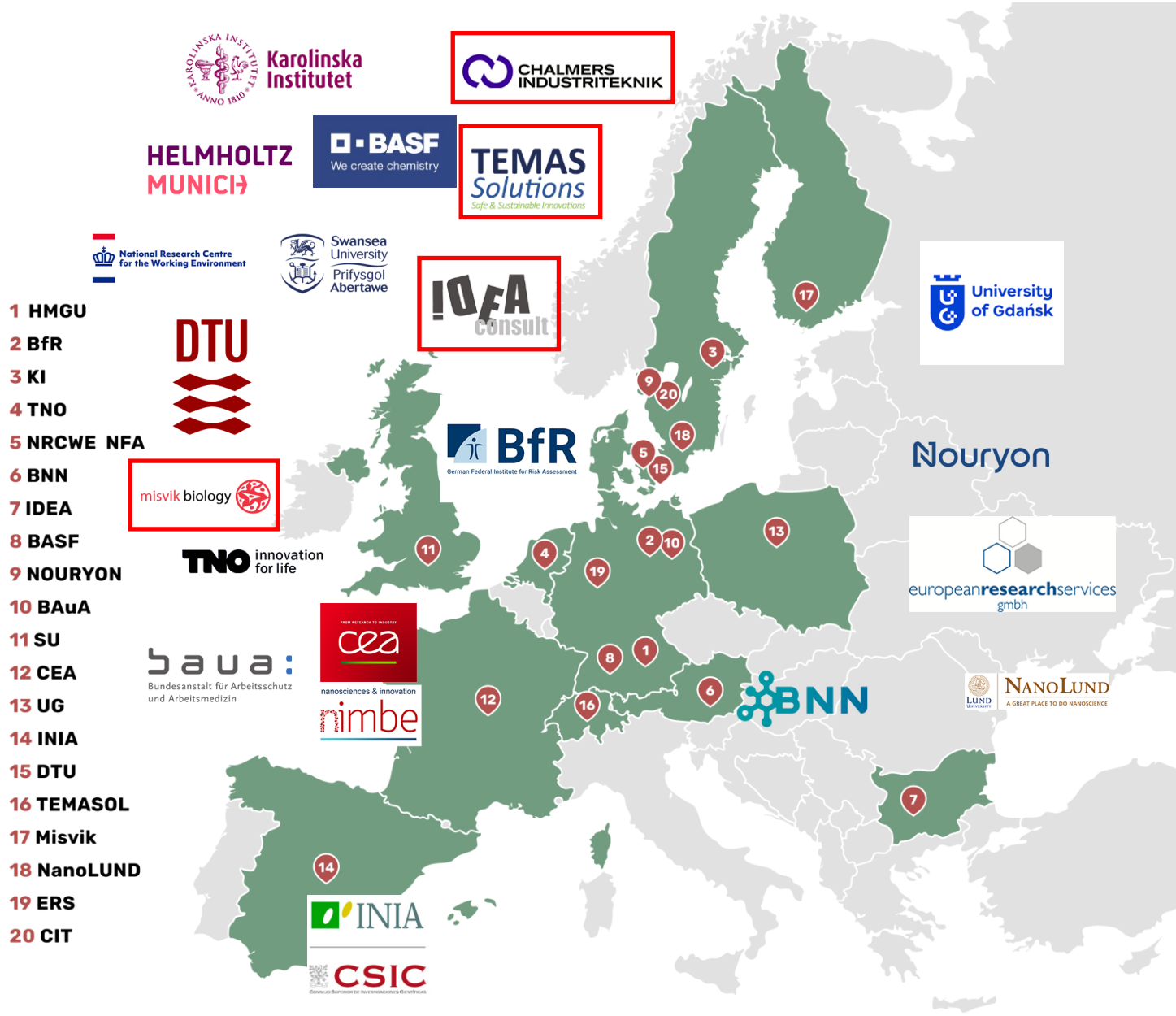
- Please choose the following “nomenclature” to present your name when logging in: SURNAME - First name – Country-company/code – Short name of your organisation (e.g., ALFARO Beatriz – AT – BNN).
- Please use a **headset and mute your microphone** if you are not speaking.
- Please **deactivate your camera** if you are not talking.
- Please **raise your hand** if you want to say something or use the **chat function**.
- If you have a **question**, please use the **chat**. Start with typing **“?”**. Based on the entries in the chat the moderator will pick up questions for further discussion within the group.

Webinar on Safe-and-Sustainable-by-Design (SSbD) for consultancy companies, SME and large industry: Demonstration of the user-friendly HARMLESS Decision Support System (DSS) with an advanced material as a case study

25th April 2024, 13:00 – 15:00h CEST - online

HARMLESS

- Call for **Safe by design**, from science to regulation: **multi-component nanomaterials** (NMBP-16)
- Duration: **49 months (Feb. 2025)**
- Consortium:
  20 Partners from 12 EU countries
  - **2 Industries (BASF, Nouryon)**
  - **4 SMEs**
- Coordinators:
  Tobias Stoeger, Otmar Schmid
  (Helmholtz Zentrum München, Germany)
- www.harmless-project.eu



Selected EU/OECD activities – Safe-and-Sustainable-by Design (SSbD)

European Green Deal (Feb 2023)

https://ec.europa.eu/clima/eu-action/european-green-deal_en

- EU Action plan "Towards a Zero Pollution for Air, Water and Soil
- The Circular Economy Action Plan
- The EU Chemicals Strategy for Sustainability Towards a Toxic-Free Environment

A pre-market approach to chemicals that focuses on providing a function (or service), while avoiding volumes and chemical properties that may be harmful to human health and the environment. (Def. of SSbD in CSS)

OECD Working Party on Manufactured Nanomat. – Steering Group on Advanced Materials (AdMa)

Advanced Materials (AdMa) are understood as materials that are rationally designed to have

- new or enhanced properties, and/or
- targeted or enhanced structural features

with the objective to achieve specific or improved functional performance (over conventional materials, CoMa)

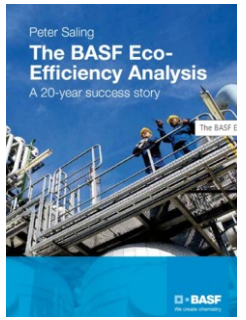
Current innovation process

Product Idea&Screening → Gate2 → Lab Scale → Gate3 → Pilot scale → Gate4

Mainly driven by
- Functionality
- Cost

Risk/Regulation

Sustainability



Launch

HARMLESS approach to SSbD: pre-market approach to AdMA-enabled products that focuses on providing function, while avoiding volumes and material properties that may be harmful to human health and the environment.

Value Proposition

Considering „safety“ and „sustainability“ during ALL phases of product development

- **Mitigate health risks** for employees, consumer, enviromment
- **Higher acceptance at market place** („sustainablility“)
- **Save money**
  - no investment in products later potentially considered „non-safe“ or „non-sustainable“
  - avoids cost for potential redesign of product
- **Later: easier regulatory acceptance (?)**

Summary of METHODOLOGY

37 New Approach Methods (NAMs) are developed for different TIER levels (*in vitro*, *in silico*)

- Hazard
- Exposure
- Internal dose
- Life Cycle Analysis
- Ecotoxicology

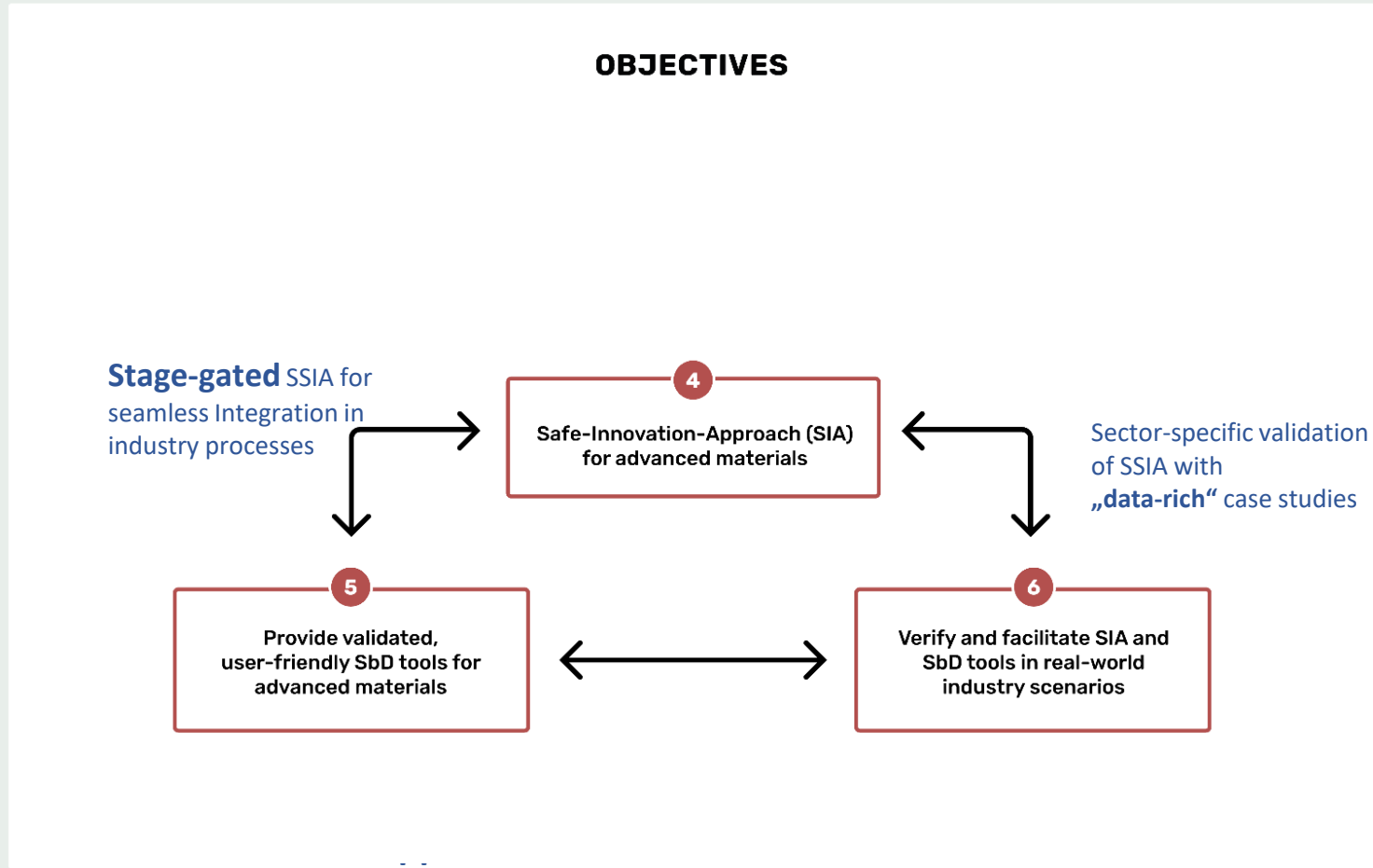
***In vivo* anchorage:**

Identified 32 Adverse Outcome Pathways (AOPs, MoA)

- 25 human health
- 7 ecotoxicology

Safety & Sustainability assessment

- Datahub for multi-scale modelling (e.g. QSARs, AI-driven approaches)
- *In vitro / in vivo* / human translation (internal dose)
- „Positioning“ of AdMa in risk and sustainability matrix

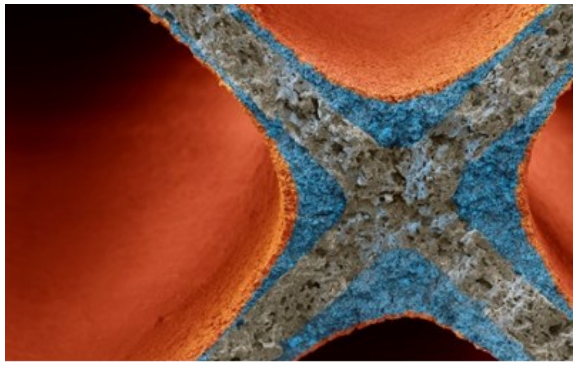


HARMLESS Case Studies

- **Sector-specific approaches**, because industry sectors differ in *functionality* and *concern*, circularity, applicable regulation, intended use by professionals or by consumers, or in the environment.

Focus of advanced case study materials

- Mixtures of (rare earth) metals/oxides
- HARN (High Aspect Ratio Nanomaterials)



CS 1 - Papermaking
Material: silica additives
Sector: manufacturing – accelerated dewatering

SiO_2
HARN

CS 2 - Paint formulations
Material: silica additives
Sector: construction – dirt repellent facades

SiO_2

CS 3 - Catalysts
Material: perovskites
Sector: automotive mobility – three-way-catalyst

La, Co, Ni, Pt, + Pd (~1%)

CS 4 - Facade insulation
Material: aerogel fibre
Sector: construction – insulation

O, Si, C, Al, Mg, Zr, Cr, Fe, Co, S, Ca, Sn, Cu,* Au*
HARN

CS 5 - Agriculture
Material: modified imogolite multi-component nanotubes
Sector: agriculture – environmental plant protection

Inorganic nanotubes: Imogolites (Al, Si) (HARN)

Objectives

- **Demonstrate the user-friendly HARMLESS decision support system (DSS)** for integration of Safe-and-Sustainably-by-Design (SDbD) principles in AdMa-enhanced product development (case study!)
- Make SSbD work for SMEs!

Agenda

13:00 - 13:05	**Introduction to the interactive webinar** by Otmar Schmid (HMGU)
13:05 - 13:15	**Overview of the HARMLESS approach to SSbD of advanced materials in product development** by Blanca Suarez (TEMASOL)
13:15- 13:25	**Introduction to perovskite case study: catalytic converter in automotive industry** by Veronica Di Battista (BASF)
13:25 - 13:45	**Demonstration of the DSS for perovskites** by Eugene van Someren (TNO)
13:45 - 14:05	**Introduction to the HARMLESS Decision Support System (DSS)** by Susan Dekkers (TNO)
14:05 - 14:50	**Interactive Q&A session** by Otmar Schmid (HMGU)
14:50 - 15:00	**Workshop wrap-up** by Otmar Schmid (HMGU)

Overview of the HARMLESS approach to SSbD of advanced materials in product development

Blanca Suarez Merino (TEMASOL)

SSbD is not regulation but a recommendation for R&D

Safe and Sustainable by Design chemicals and materials

Framework for the definition of criteria and evaluation procedure for chemicals and materials

Draft Report for consultation

Caldeira, C. Farcal, L., Tosches D., Amelio, A., Rasmussen, K., Rauscher, H., Riego Sintes, J., Sala, S.

2022

unmz

New Work Item Proposal	
Safe-and-Sustainable-by-Design concept dedicated to nano scale materials (MNM) and products containing nanomaterials	
CEN/TC 352 – Nanotechnologies	
Secretariat: AFNOR	Proposal documented in N xx To be completed by CEN/TC 352 secretary
Date of circulation: To be completed by CEN/TC 352 secretary	Closing date for voting: To be completed by CEN/TC 352 secretary

Proposal

0. This proposal relates to

- ☐ the creation of a new project in the committee's work programme (stage 10.99)
- ☒ the creation of a preliminary project in the committee's work programme (stage 00.60)
- ☐ the activation of a project currently registered as a Preliminary Work Item in the committee's work programme: PWI XXXXX

1. Deliverable

- ☐ European Standard (EN)
- ☐ Harmonization Document (HD) – *for CENELEC only*
- ☒ Technical Specification (TS)
- ☐ Technical Report (TR)

2. This item corresponds to

- ☒ A new project
- ☐ An amendment to the EN XXX
- ☐ The revision of EN XXX
- ☐ The conversion of TS XXX into an EN
- ☐ The conversion of ENV XXX into an EN
- ☐ The revision of TS XXX
- ☐ The revision of TR XXX

3. Explain the purpose and give a justification for this proposal

Safe-by-Design (SbD) is a well-established concept first proposed in 19xx in technical fields like construction, nuclear technology, water treatment, health facilities, and occupational health and safety (Ref). Many definitions of SbD can be found in the literature for material/chemical engineering, and some focus on nanomaterials. SbD is typically driven by regulatory requirements and soft regulation, governance information, sustainability analysis & life cycle analysis (LCA),

EUROPEAN COMMISSION

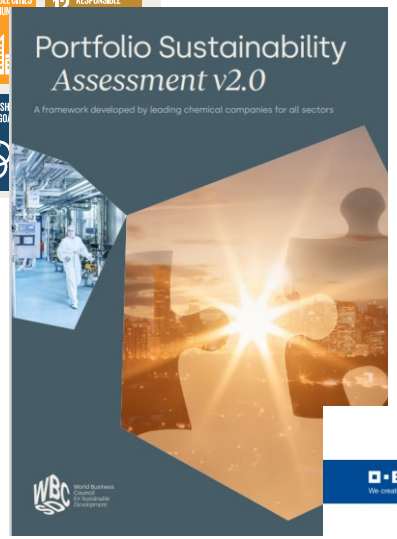
Brussels, 8.12.2022
C(2022) 8854 final

COMMISSION RECOMMENDATION

of 8.12.2022

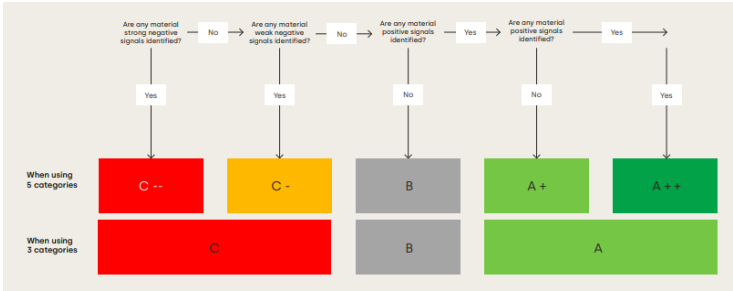
…opean assessment framework for 'safe and sustainable by design' chemicals and materials

Sustainability strategies used by industry



Portfolio sustainability Assessment v2.0

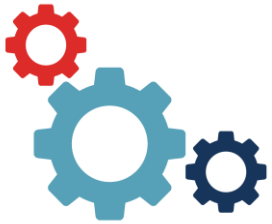
Decision tree for weighting and ranking material's versions



BASF
We create chemistry

Current innovation process

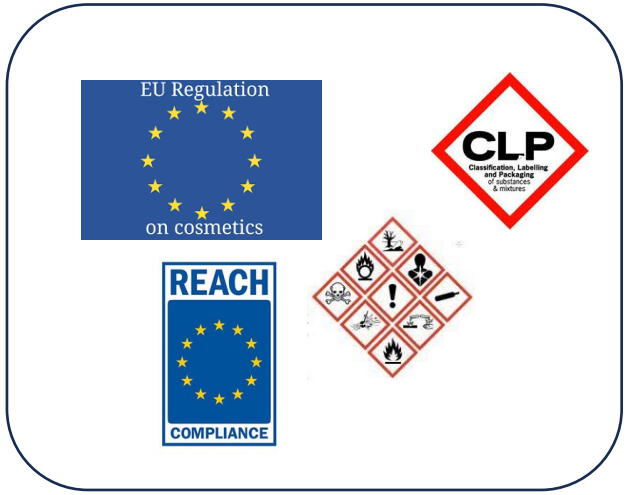
Product Idea&Screening → Gate2 → Lab Scale → Gate3 → Pilot scale → Gate4

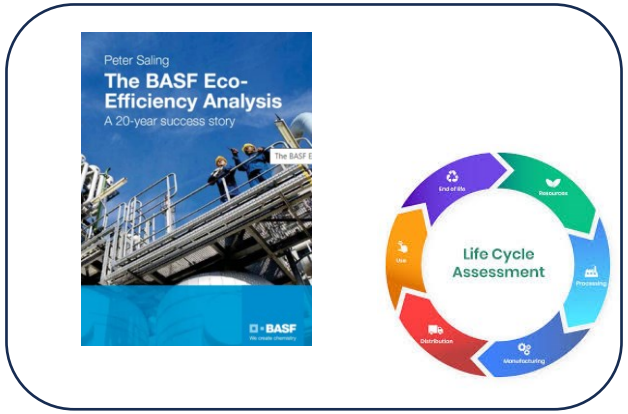


Functionality driven

Regulation

Sustainability





~2% of ideas make it to market launch

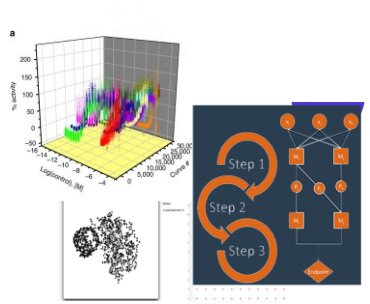
The Harmless SSbD Approach

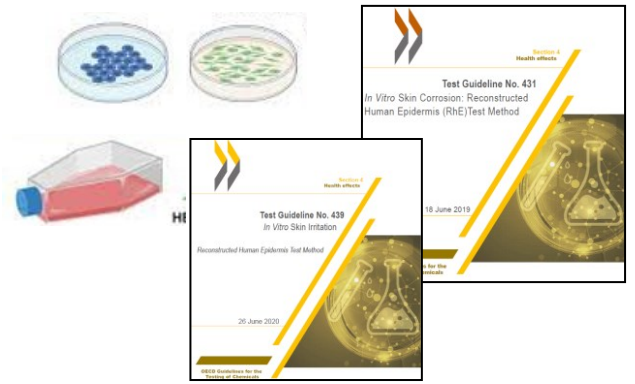
Lack of data availability

Qualitative assessment

Quantitative assessment

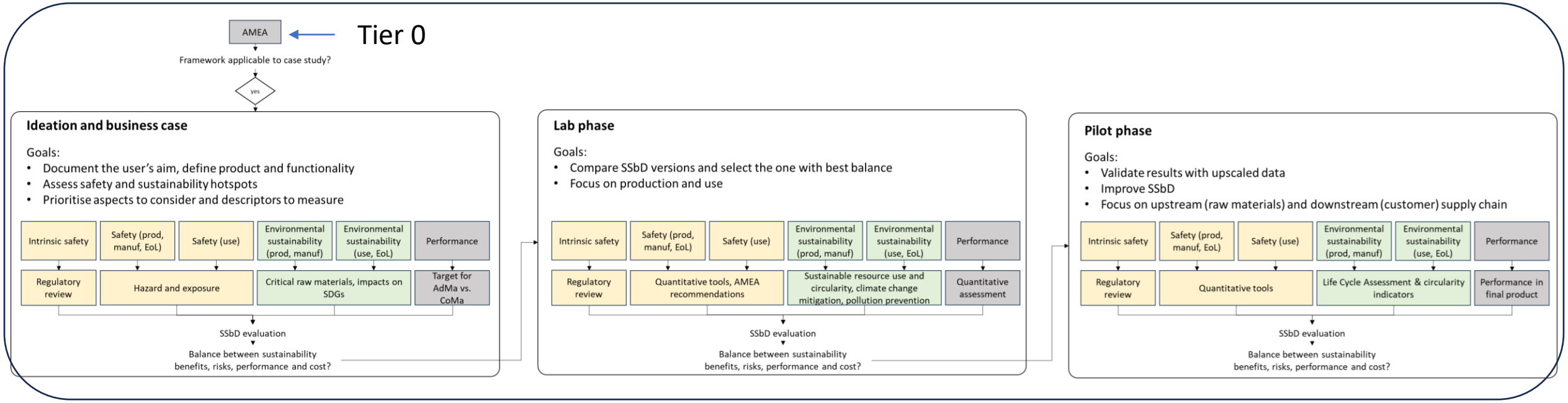
Tools





SSbD anticipates regulatory needs following a cost-effecting testing approach

The HARMLESS SSbD Framework



Design Principles
Approaches, Methods and tools

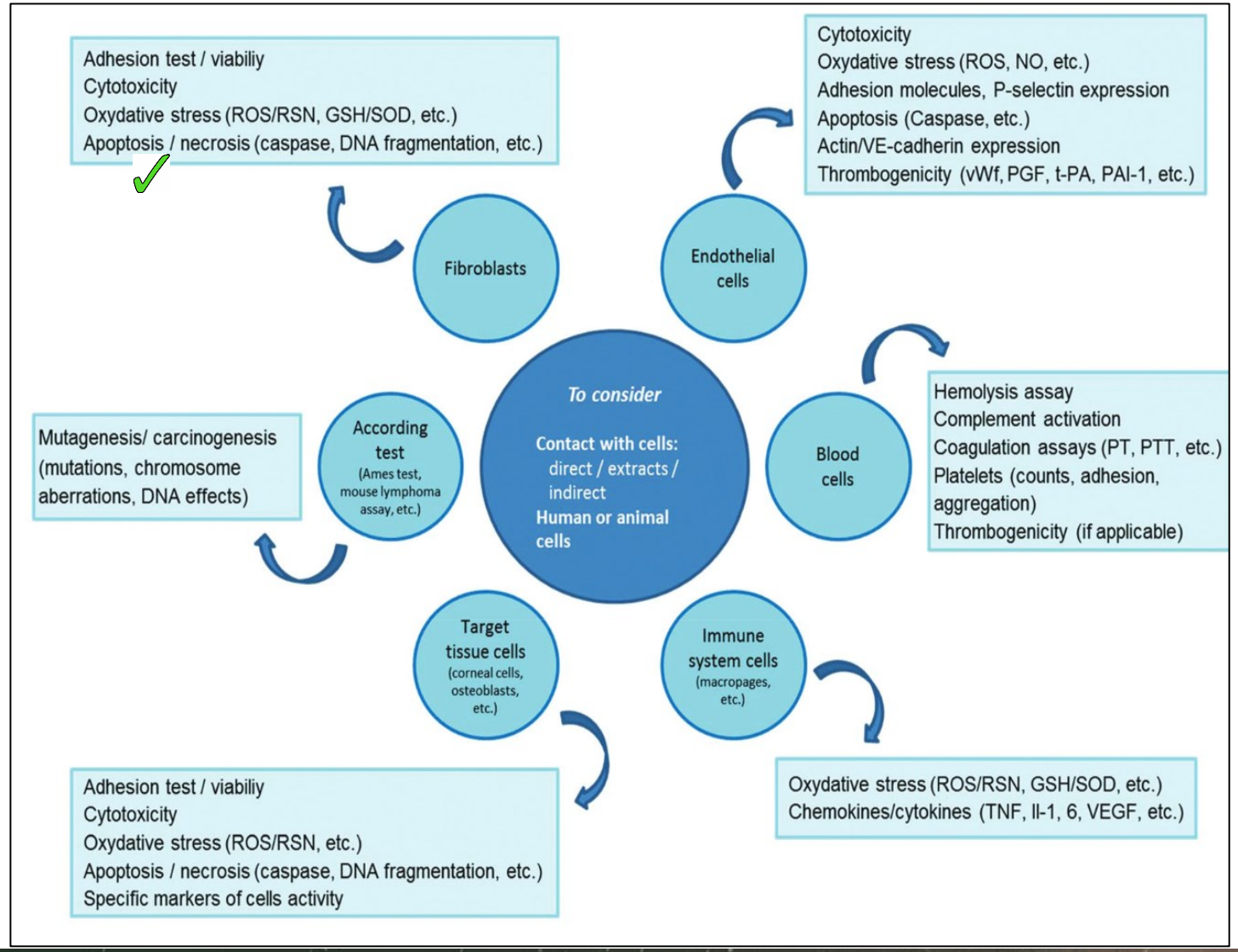
Design Principles
Approaches, Methods and tools

Design Principles
Approaches, Methods and tools

Implemented as a Decision Support System

How to implement SSbD?

Selection of most promising materials (Safety and functionality)



HARMLESS DSS

Tier 0

AMEA → 3 questions

Ideation

WASP → 14 questions

Lab

ASDI → Measured descriptor values

Introduction to the perovskite case study: catalytic converter in automotive industry

Veronica di Battista (BASF)

Catalysts based on perovskites

Catalysts based on perovskites

Design space

Functionality

Issues/Concerns

Design space

- Composition, crystallinity, size, surface area

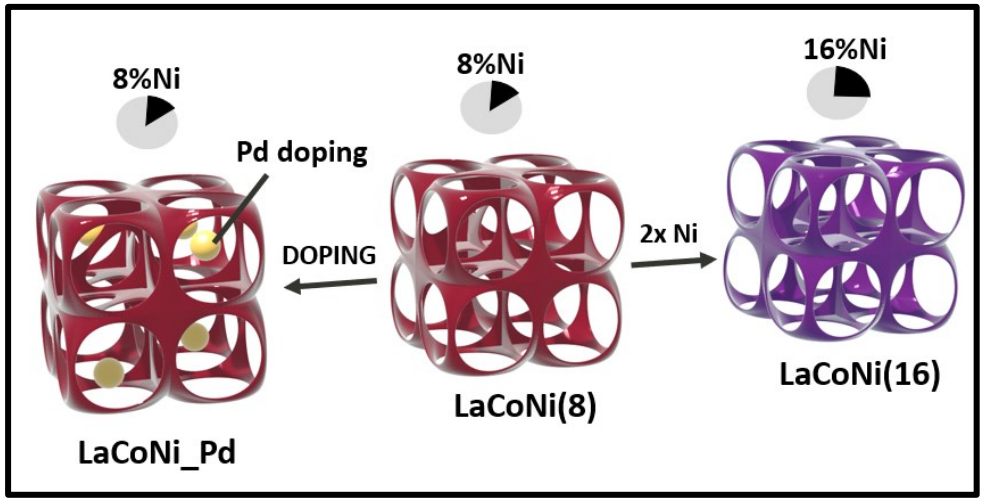
Design space

- Composition, crystallinity, size, surface area → **influence** conduction/valence band level, band gap

Design space

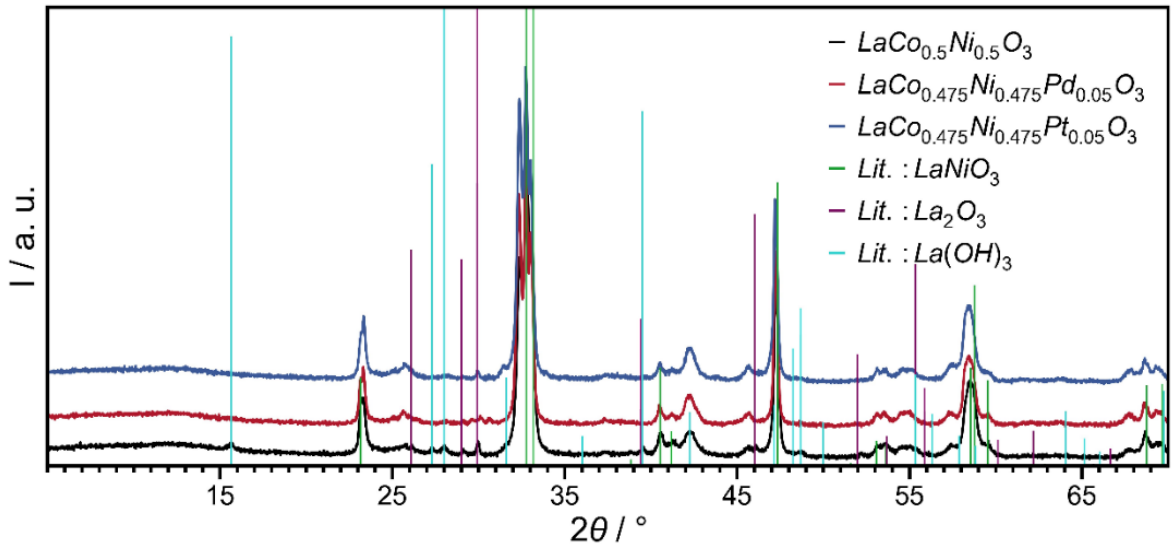
- Composition, crystallinity, size, surface area
- Nickel/Cobalt content variation and doping

Material	Co%wt	La%wt	Ni%wt	Pd%wt	Pt%wt
LaCoNi(8)	12.0	60	**8.0**	/	/
LaCoNi_Pd	12.0	60	**7.9**	**0.59**	/
LaCoNi_Pt	12.0	60	**7.5**	/	**1.1**
LaCoNi (5)	17.6	57	**5.1**	/	/
LaCoNi (16)	6	58	**16**	/	/
LaNi (22)	/	59	**22**	/	/



Design space

- Composition, crystallinity, size, surface area
- ABO_3 structure were A = **La** , B = **Co** and **Ni +** doping by **Pt** and **Pd** (in less than 1%wt)



Design space

- Composition, crystallinity, size, surface area
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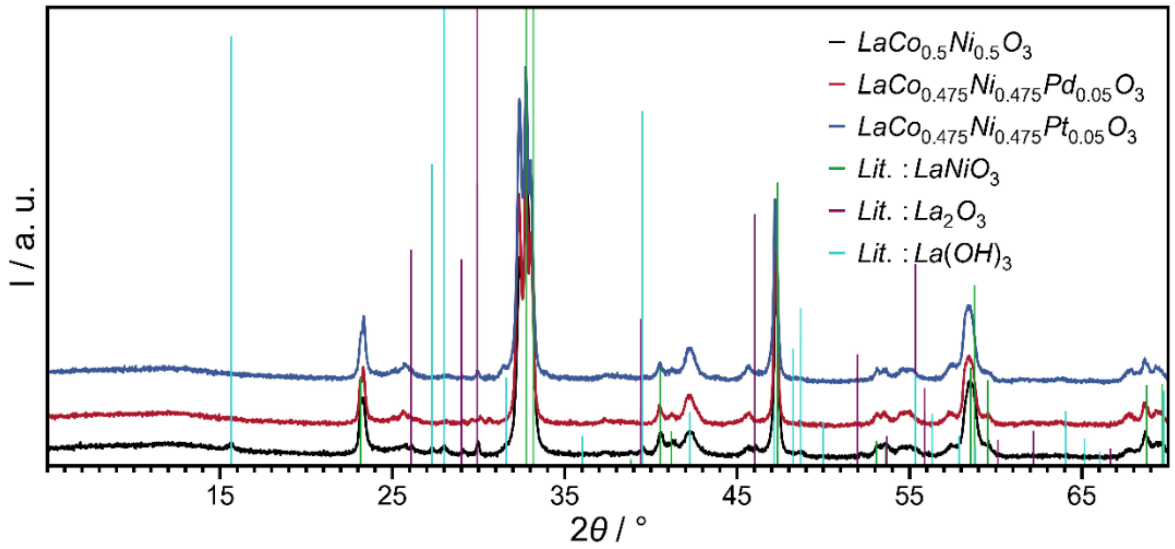
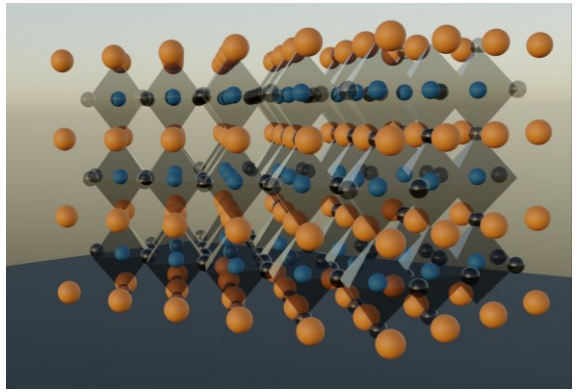


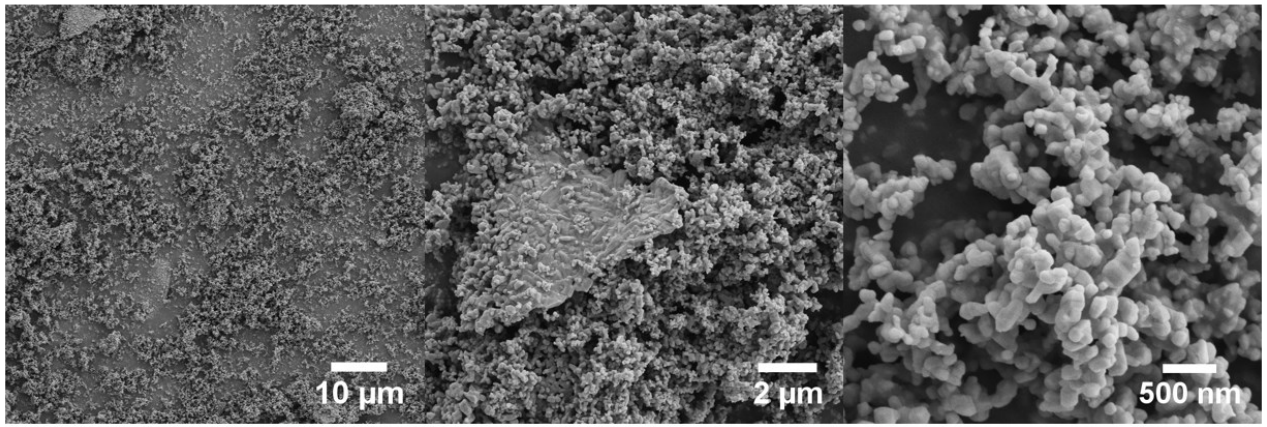


Perovskite-like pseudo cubic crystal structure

Design space

- Composition, crystallinity, size, surface area
- Not nano by REACH definition but nano enabled by ISO definition

Material	BET (m^2/g)	Min Feret in nm (SEM, median)
LaCoNi(8)	3.8	96
LaCoNi_Pd	2.3	206
LaCoNi_Pt	4.6	107
LaCoNi (5)	2.8	121
LaCoNi (16)	3.7	123
LaNi (22)	4.0	129



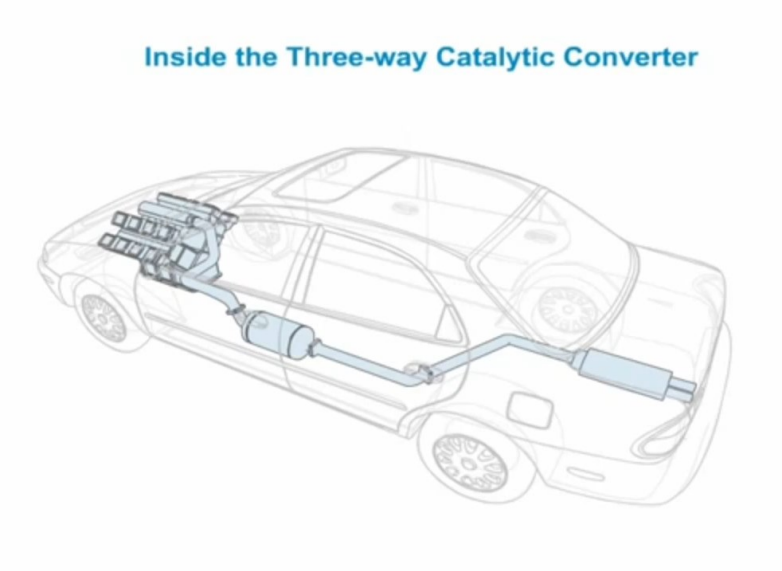
Design space

Functionality

Issues/Concerns

Intended functionality

- Component of three-way catalyst for the conversion of pollutants in the car exhaust
- Enhance catalyst turnover activity and increase oxygen storage capacity



The product aims to provide a positive contribution to Sustainable Development Goal 11, by improving air quality with high performance catalysts

Catalysts based on perovskites

Design space

Functionality

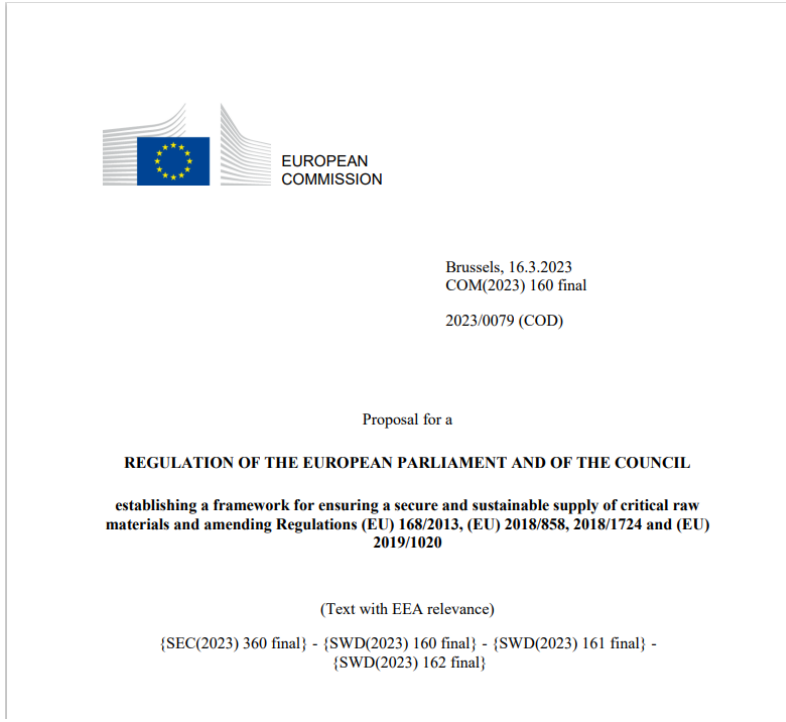
Issues/Concerns

Issues/possible concerns

- Co and Ni are regulated under CLP as known carcinogens

- Perovskites are multi component, therefore mixture effects should not be overlooked (i.e., chemical transformation)
- Co, Ni, Pd, Pt are all known Critical Raw Materials

Material	Code	Hazard Statement
Ni CAS No: 7440-02-0	H317 H351 H372	Sensitisation — Skin, Hazard Category 1 Carcinogenicity, Hazard Category 2 Specific target organ toxicity — Repeated exposure, Hazard Category 1
Co CAS No: 7440-48-4	H317 H334 H341 H350 H360 H413	Sensitisation — Skin, Hazard Category 1 Sensitisation — Respiratory, Hazard Category 1 Germ cell mutagenicity, Hazard Category 2 Carcinogenicity, Hazard Category 1A, 1B Reproductive toxicity, Hazard Category 1A, 1B Hazardous to the aquatic environment - Chronic Hazard, Category 4



EUROPEAN COMMISSION

Brussels, 16.3.2023
COM(2023) 160 final

2023/0079 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

establishing a framework for ensuring a secure and sustainable supply of critical raw materials and amending Regulations (EU) 168/2013, (EU) 2018/858, 2018/1724 and (EU) 2019/1020

(Text with EEA relevance)

{SEC(2023) 360 final} - {SWD(2023) 160 final} - {SWD(2023) 161 final} - {SWD(2023) 162 final}

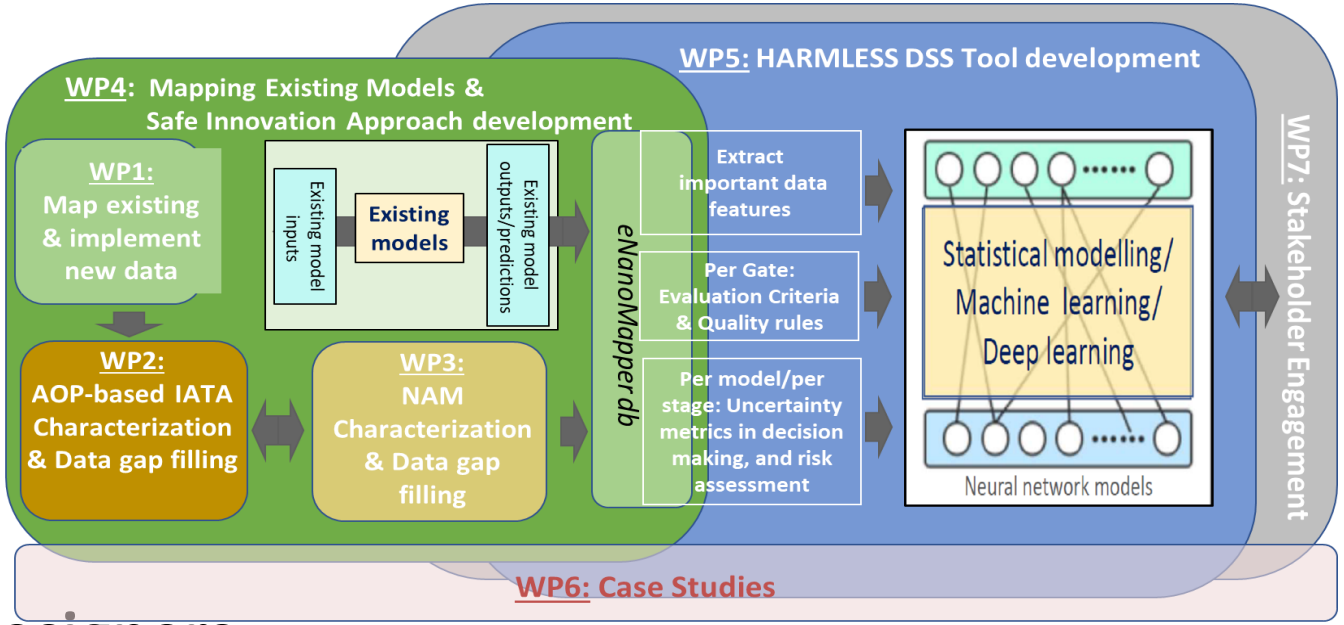
HARMLESS

Introduction to the HARMLESS Decision Support System

Eugene van Someren (TNO)

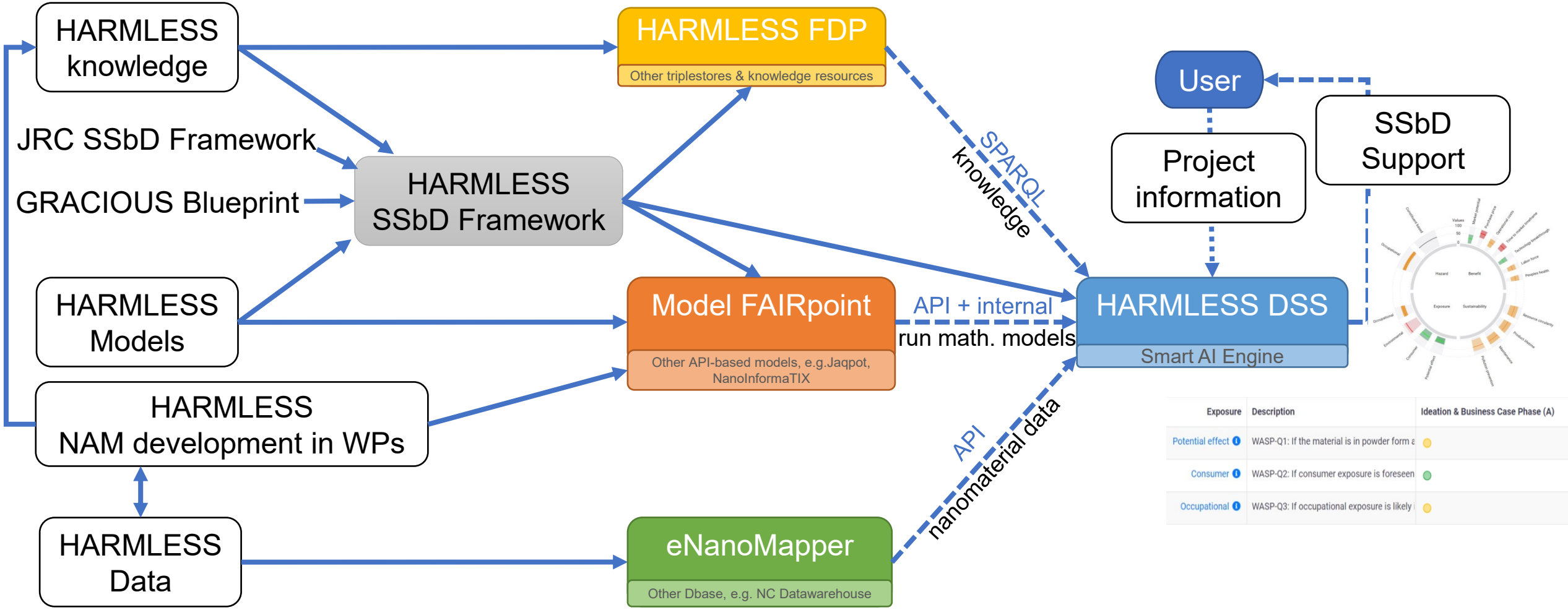
Objectives of the Decision Support System (SSbD-DSS)

Build a user-friendly Decision Support System based on SSbD Framework

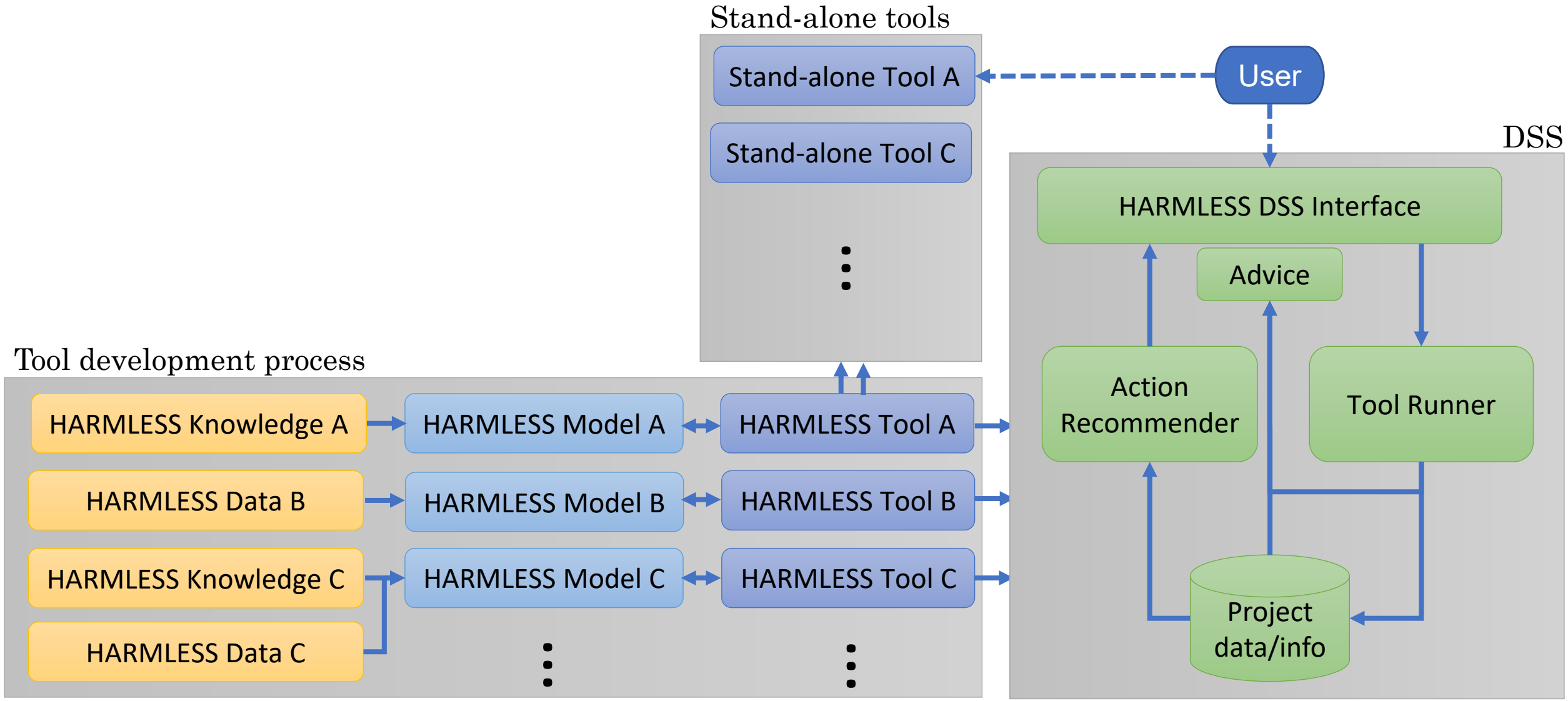


- **Industrial (innovative material) designers**
- **Advanced (nano)materials (complex HARNs & MC ENMs)**
- **Innovation stages and life cycle stages**
- **Integration knowledge, models and data (within the DSS)**

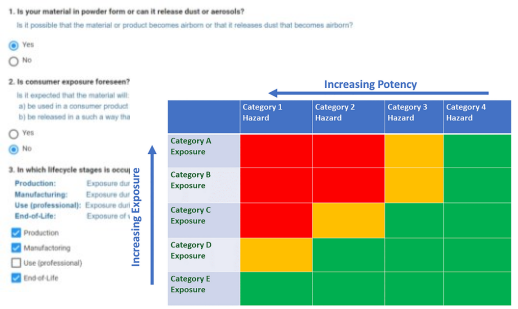
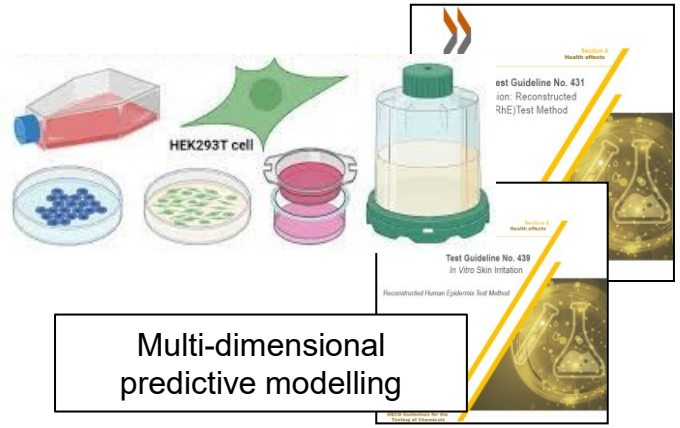
FAIR & Modular Architecture



Sustainable & Modular Tool Development Platform



The Safe and Sustainable by Design Approach

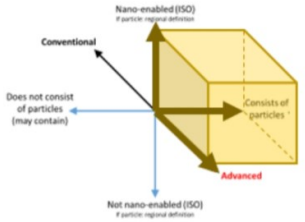
Innovation Stage	Ideation & business case	Lab phase	Pilot phase
Stage's Aim	Early Warning & Design principles	Comparing SSbD versions	Assessment of chosen SSbD version
Data availability	Qualitative assessment		Quantitative assessment
DSS approach	Simple questions & decision logic	Measurements & Visualization	Higher-Tiered Measurements & Predictions
Methods, Tools & NAMS			
	Substances Information System (for hazard banding)	Dissolution in relevant media Acellular (bio)reactivity	Multi-dimensional predictive modelling

SSbD Tools in the Decision Support Systems

Innovation Stage	Ideation & business case	Gate2	Lab phase	Gate3	Pilot phase	Gate4
Stage's Aim	Early Warning & Design principles		Comparing SSbD versions		Assessment of chosen SSbD version	
Data availability	Qualitative assessment				Quantitative assessment	

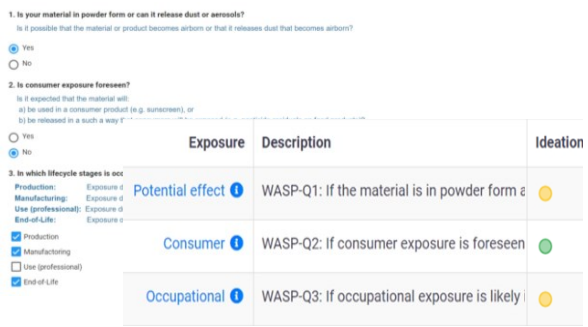
AMEA

Categorization
Design principles



WASP

Early Warning, SSbD advice and Assessment Advice

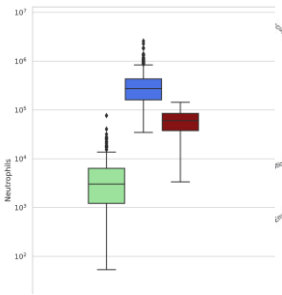


ASDI

Measured Descriptors for diverse dimensions

Advanced descriptors Higher-tiered Tools

Predictive in-vivo risk models based on physchem, in chemico and in vitr



Recommended Workflow

AMEA = Advanced Material Earliest Assessment
WASP = Warning flags, design Advice, Screening Priorities
ASDI = Alternative SSbD Design Inspector

Start: Create new DSS Project

3 questions → AMEA → AMEA Category, Design Principle Advice

If applicable category

Ideation & business case

14 questions → WASP → Early Warning flags (Criteria Checker), Design Advice, Assessment Advice (incl. suggested descriptors)

Ready for lab phase

Lab phase

AdMa, CoMa, Ref Designs
Measured descriptor values → ASDI → Interactive Comparative Visualization, Descriptor-specific Advice

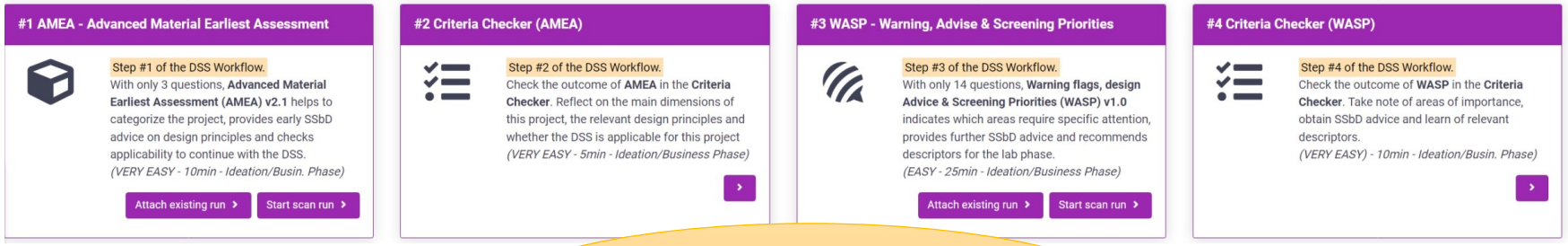
Selected SSbD Design
Ready for pilot phase

Pilot phase

WORK IN PROGRESS

Advanced descriptors
Higher-tiered Tools ↔ Nano Exposure Quantifier, QSAR, Bayesian Network & weighted SVM-based Prediction based on HARMLESS in chemico/vitro/vivo LT/HT/Omics data

The SSbD-DSS guides you through iterations



Start: Create new DSS Project

Project Dashboard

Recommended Actions

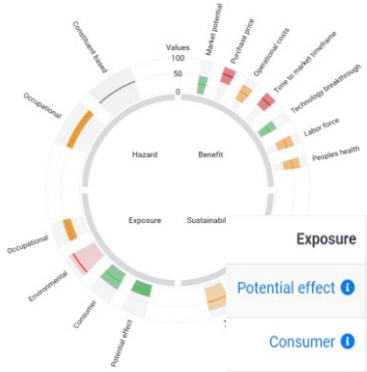
DSS iterations

Inspect Results

- Visualization
- Advice

Perform Action

- Run a Tool
- Add data/info



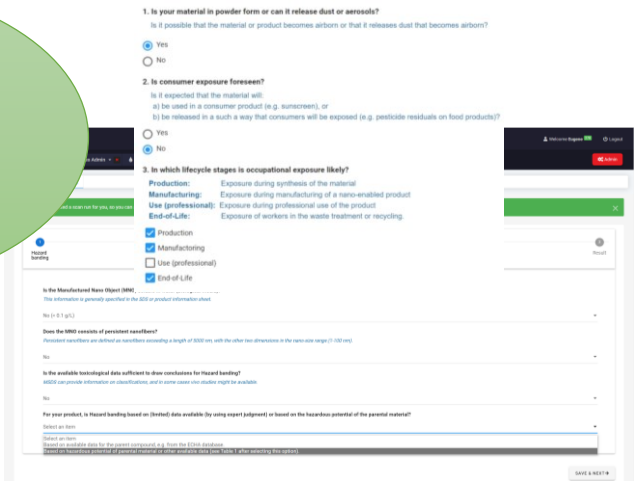
Exposure	Description	Ideation
Potential effect	WASP-Q1: If the material is in powder form a	
Consumer	WASP-Q2: If consumer exposure is foreseen	
Occupational	WASP-Q3: If occupational exposure is likely	

Exposure during Lifecycle

Design principles focus on circularity. The intended use that is captured by the P-A-R allows a qualitative identification of hot spots, where emission into the environment and/or exposure of humans is likely. Often times, these hot spots are well known in the industry sector.

Design principles:

- Consider EoL, design for circularity
- Describe P-A-R = product, application, region (World_Business_Council_for_Sustainable_Development 2018) and qualitatively identify potential hot spots



Follow the list of recommended actions (purple) or feel free to choose optional actions (brown)

Show Support

Recommended actions

Find below the currently most recommended actions to do. Below the available actions are presented in recommended order.

#1 AMEA - Advanced Material Earliest Assessment

Step #1 of the DSS Workflow.
With only 3 questions, **Advanced Material Earliest Assessment (AMEA) v2.1** helps to categorize the project, provides early SSbD advice on design principles and checks applicability to continue with the DSS.
(VERY EASY - 10min - Ideation/Busin. Phase)

Attach existing run › | Start scan run ›

#2 Criteria Checker (AMEA)

Step #2 of the DSS Workflow.
Check the outcome of **AMEA** in the **Criteria Checker**. Reflect on the main dimensions of this project, the relevant design principles and whether the DSS is applicable for this project
(VERY EASY - 5min - Ideation/Business Phase)

›

#3 WASP - Warning, Advise & Screening Priorities

Step #3 of the DSS Workflow.
With only 14 questions, **Warning flags, design Advice & Screening Priorities (WASP) v1.0** indicates which areas require specific attention, provides further SSbD advice and recommends descriptors for the lab phase.
(EASY - 25min - Ideation/Business Phase)

Attach existing run › | Start scan run ›

#4 Criteria Checker (WASP)

Step #4 of the DSS Workflow.
Check the outcome of **WASP** in the **Criteria Checker**. Take note of areas of importance, obtain SSbD advice and learn of relevant descriptors.
(VERY EASY) - 10min - Ideation/Busin. Phase)

›

Optional actions (future actions that are not yet applicable or actions recommended only for very experienced DSS users)

#5 Advance to Lab Phase

Step #5 of the DSS Workflow.
When AMEA and WASP are finalized and the "Ideation and Business Case Phase" successfully completed, advance this projects innovation stage to the **Lab Phase**.
(VERY EASY - 1min - Ideation/Business Phase)

›

#6 ASDI - Alternative SSbD Design Inspector

Step #6 of the DSS Workflow.
Specify your SSbD designs and descriptors in the **Design page**. Enter measured values to interactively visualize design differences and get relevant SSbD advice.
(MEDIUM - 45min - Lab Phase)

›

#7 Advance to Pilot Phase

Step #7 of the DSS Workflow.
When ASDI is finalized and the "Lab Phase" successfully completed, advance this projects innovation stage to the **Pilot Phase**.
(VERY EASY - 1min - Lab Phase)

›

View the Status Wheel and Criteria Checker

The Status Wheel and/or Criteria Checker visualisation has been updated. Check these visualizations to gain insight in your SSbD status

View statuswheel ›

Stoffenmanager Nano hazard (SMnanoHaz)

SMnanoHaz determines a quick (Tier-1) hazard

Stoffenmanager Nano Exposure (SMnanoExp)

SMnanoExp determines a quick (Tier-1)

LICARA nanoScan

LICARA nanoScan allows a preliminary but

Bayesian Network SMnanoExp & NEQ (BNexposure)

A Bayesian Network model (BN) that integrates

#1 AMEA - Advanced Material Earliest Assessment

Step #1 of the DSS Workflow.

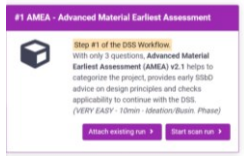
With only 3 questions, **Advanced Material Earliest Assessment (AMEA) v2.1** helps to categorize the project, provides early SSbD advice on design principles and checks applicability to continue with the DSS.

(VERY EASY - 10min - Ideation/Busin. Phase)

Attach existing run › Start scan run ›

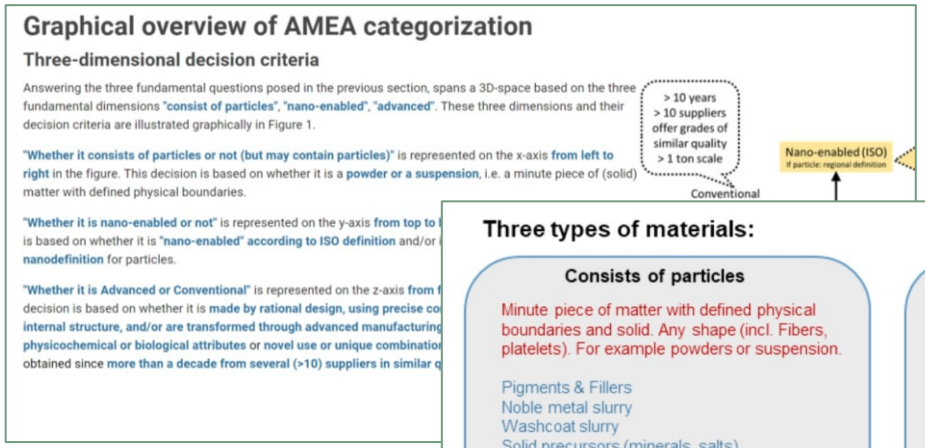
Describe difficulty, time and stage for each action

Start action

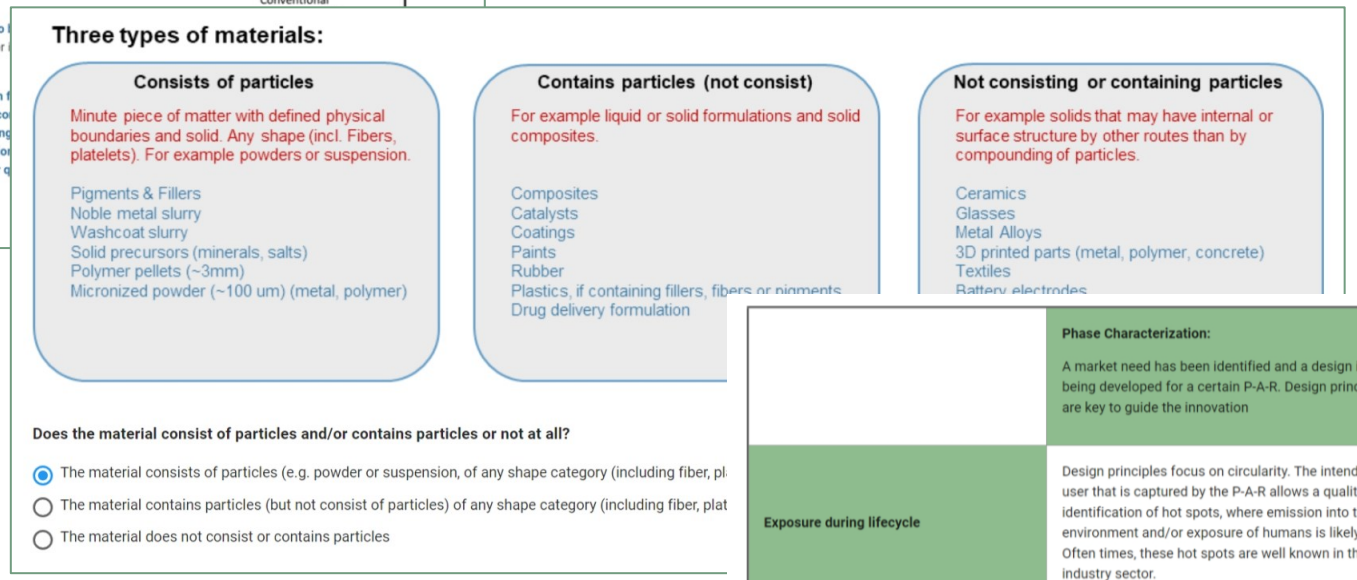


AMEA in the SSbD-DSS as an Example

Introduction pages



Answer Questions



Resulting Advice

	Phase Characterization: A market need has been identified and a design is being developed for a certain P-A-R. Design principles are key to guide the innovation	Guidance for Assessment:
Exposure during lifecycle	Design principles focus on circularity. The intended user that is captured by the P-A-R allows a qualitative identification of hot spots, where emission into the environment and/or exposure of humans is likely. Often times, these hot spots are well known in the industry sector.	**Design Principles:** • Consider EoL, design for cicularity • Describe P-A-R = product, application, region (World_Business_Council_for_Sustainable_Development 2018) and qualitatively identify potential hot spots
Hazard	Design principles focus on warning signs from late lessons to early warnings: (Harremoës *et al.* 2001) (Table 2)	**Design principles from late lessons to early warnings: (Harremoës) *et al.* 2001)** • Fibers fitting the WHO criteria (HARM) • Persistancy, widespread use • Bioaccumulation, irreversible effects • Heavy metals & other GRA groups • Novelty (= trigger of AdMa discussion)
Sustainability	Design principles of the AdMa product are derived from the sustainability deficiencies of the CoMa product for the same A-R target	

Recommended Actions updated

Back to SSbD-DSS

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TNO innovation for life

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DIAMONDS

A GENERIC DATA MANAGEMENT AND INTEGRATION PLATFORM FOR THE LIFE SCIENCES

DIAMONDS brings together Data, Knowledge and Algorithms. Data ranges from Clinical studies and Omics data to Personalized Health data. Traceable from original Raw measurements to Cleaned, Processed data ready to use. Knowledge ranges from Biological Knowledge from Curated databases and Textmining to manually Curated Triples from our Experts. All captured and connected to Source information through Standardized Pipelines and Workflows Protocols. Diverse tools and algorithms such as Statistical tools, Text mining methods, Scripts, Decision Trees, Bayesian/Dynamic Networks and Network Visualization.

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DIAMONDS highlights

Summary of highlighted projects and modules in DIAMONDS

Project 01-02-2023

HARMLESS

The HARMLESS project aims to develop a Decision Support System for Safe-by-Design for complex nano-materials and high-aspect ratio nano-materials.

Read more

Project 03-07-2018

Substance Information System

Substance Information System (SIS) is a public tool developed on the TNO DIAMONDS platform that allows users to search and find information on hazardous substances. The tool collects and organizes information from diverse sources to provide an integrative resource on substance properties, safety, health effects, exposure, and application by business sectors.

Read more

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Please login with your DIAMONDS account

Username * Your username

Password * Your password

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Activate public account

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collaborate

Private access

Available today for you!

ECEL | LICARA

soon

AMEA

Hotspot Scan | SIS

Jan 2025

SSbD-DSS

...

...

Diamonds 3

Welcome **Harmless** Logout

Dashboard | Select a project | Select a module

Private projects

Publicly available tools

Contamination Estimate Calculator

The contamination estimate tool provides a first indication of the unintended allergen presence (UAP) in a product .

Free publicly available tools on the DIAMONDS platform (https://diamonds.tno.nl)

Substance Information System

Welkom in het stoffeninformatiesysteem (SIS), een tool ontwikkeld door TNO en gefinancierd door ministerie SZW. SIS is ontwikkeld om een breed scala aan informatie over gevaarlijke stoffen bijeen te brengen. De tool bevat onder andere

ECEL 3.0

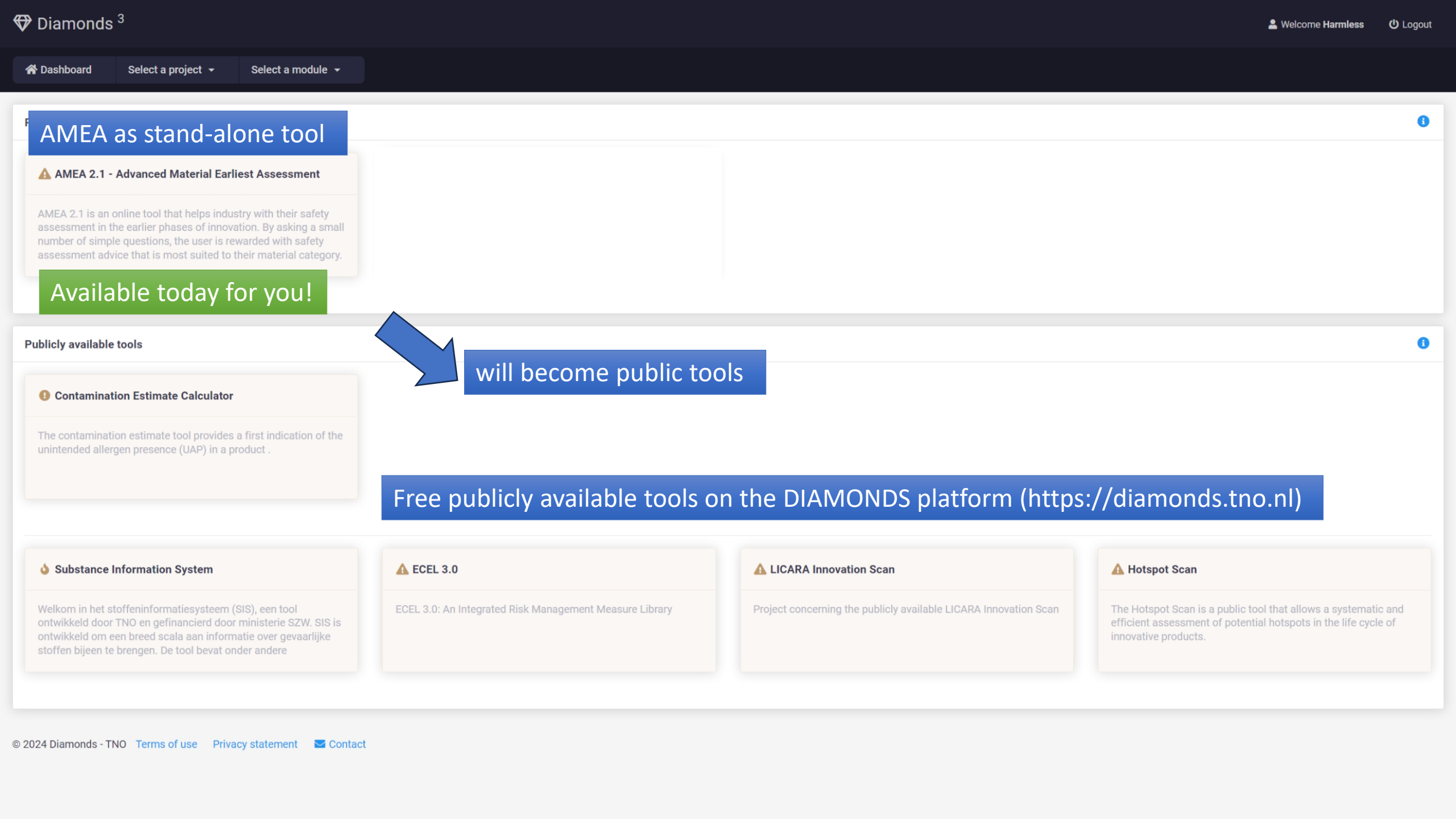
ECEL 3.0: An Integrated Risk Management Measure Library

LICARA Innovation Scan

Project concerning the publicly available LICARA Innovation Scan

Hotspot Scan

The Hotspot Scan is a public tool that allows a systematic and efficient assessment of potential hotspots in the life cycle of innovative products.


Diamonds 3
Welcome Harmless
Logout
Dashboard
Select a project
Select a module
AMEA as stand-alone tool
AMEA 2.1 - Advanced Material Earliest Assessment
AMEA 2.1 is an online tool that helps industry with their safety assessment in the earlier phases of innovation. By asking a small number of simple questions, the user is rewarded with safety assessment advice that is most suited to their material category.
Available today for you!
Publicly available tools
will become public tools
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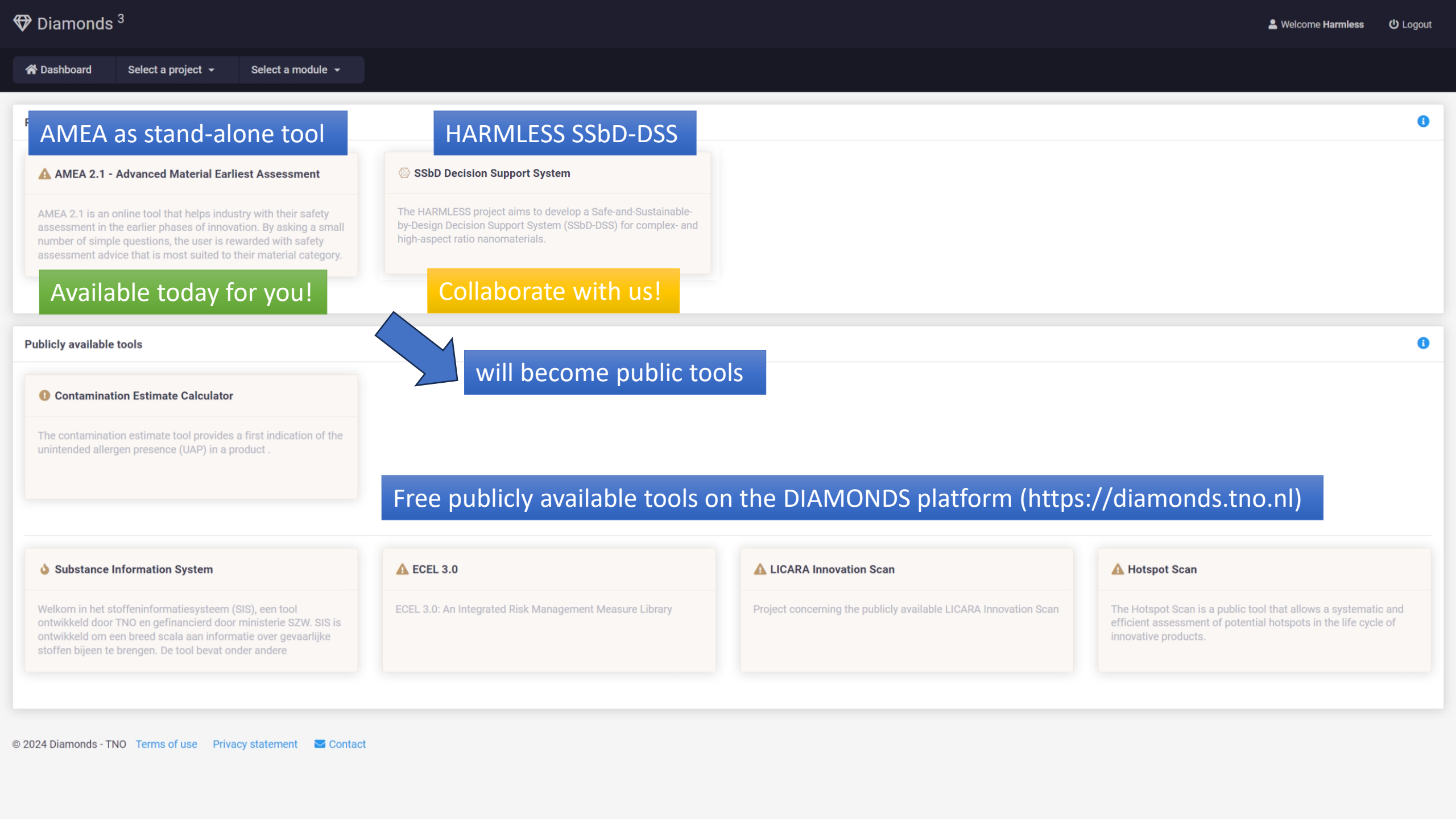
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SSbD Decision Support System
The HARMLESS project aims to develop a Safe-and-Sustainable-by-Design Decision Support System (SSbD-DSS) for complex- and high-aspect ratio nanomaterials.
Available today for you!
Collaborate with us!
Publicly available tools
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Recap

- **Principles behind the HARMLESS SSbD-DSS**
  - FAIR, Modular, Tools + Guidance, Workflow through Innovation Stages,
- **Collaboration and Access**
  - Public tools, …. + AMEA, +…, +SSbD-DSS
  - Collaborate and gain early access
  - This afternoon: sneak peak of AMEA

Collaborate with us to gain early access to the DSS!

Available today for you!

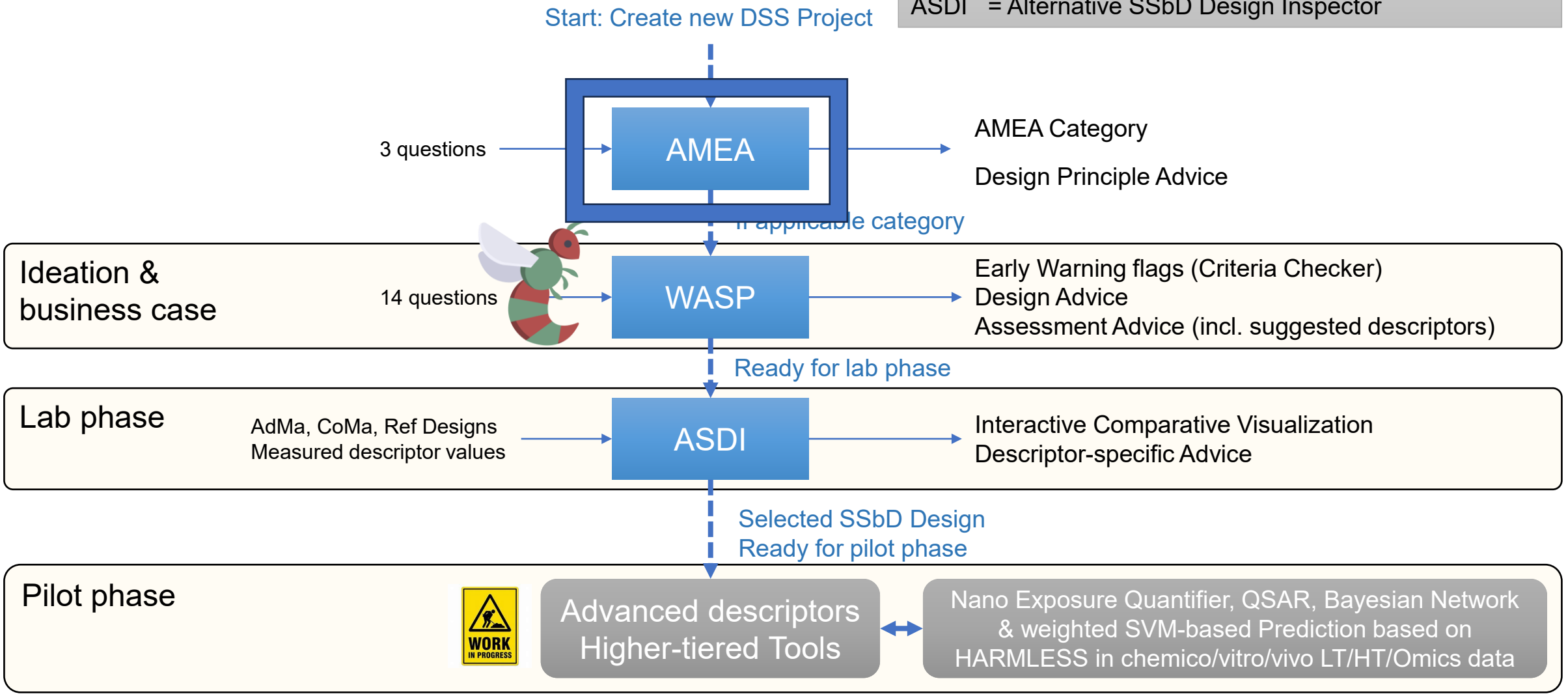
- **More about the actual contents of the SSbD-DSS in next presentations!**
  - Perovskite use-case
  - Showing the SSbD-DSS steps with the use-case

Demonstration of the DSS for perovskites

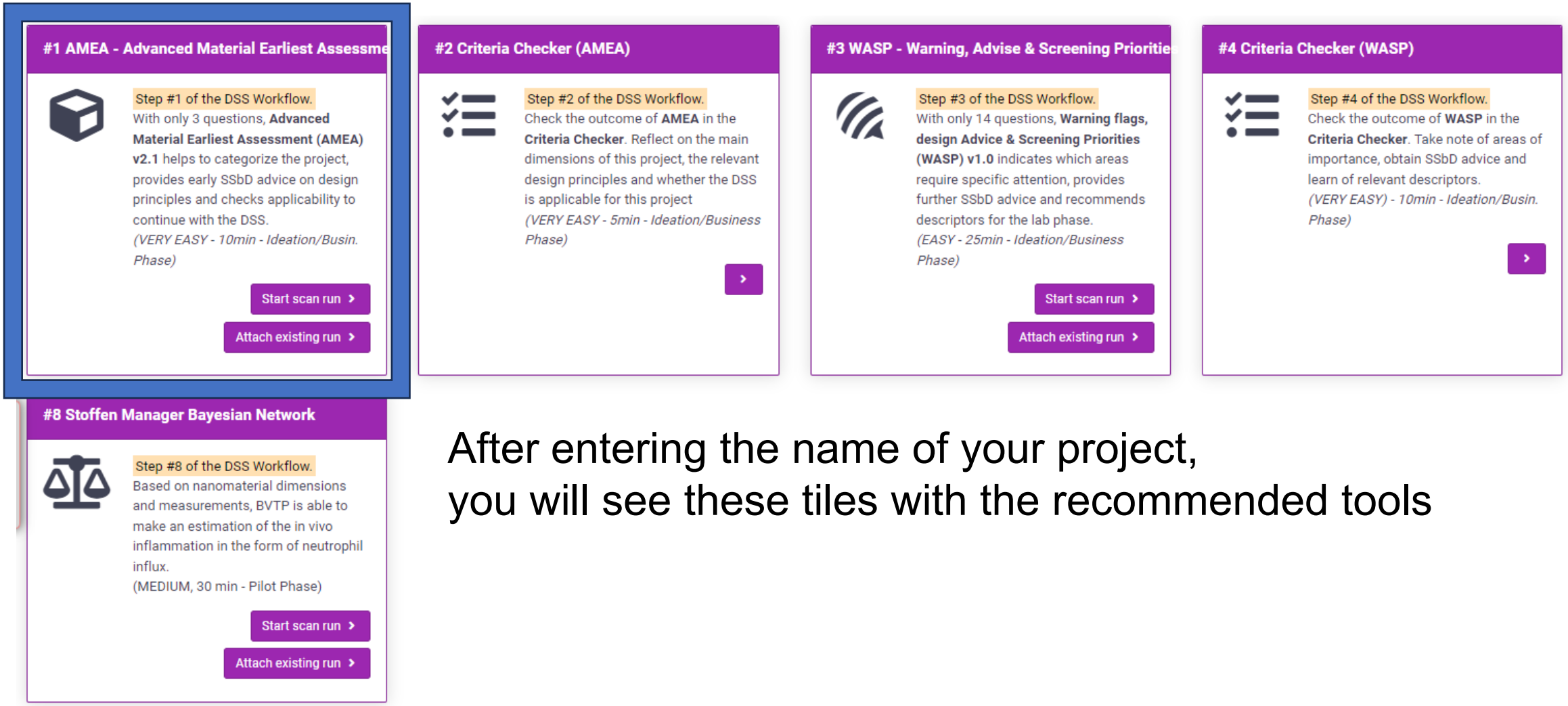
Susan Dekkers (TNO)

Workflow DSS

AMEA = Advanced Material Earliest Assessment
WASP = Warning flags, design Advice, Screening Priorities
ASDI = Alternative SSbD Design Inspector



Workflow DSS in the tool



After entering the name of your project,
you will see these tiles with the recommended tools

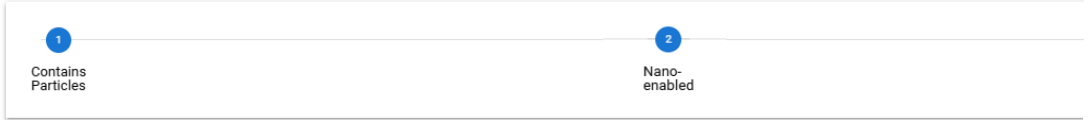
CASE STUDY PEROVSKITES FOR CATALYSIS

CS 3 - Catalysts

Material: perovskites

Sector: automotive mobility – three-way-catalyst

AMEA questions



Three questions:

1. **Does it contain/consist of particles?**
2. **Is it nano-enabled?**
3. **Is it considered advanced?**

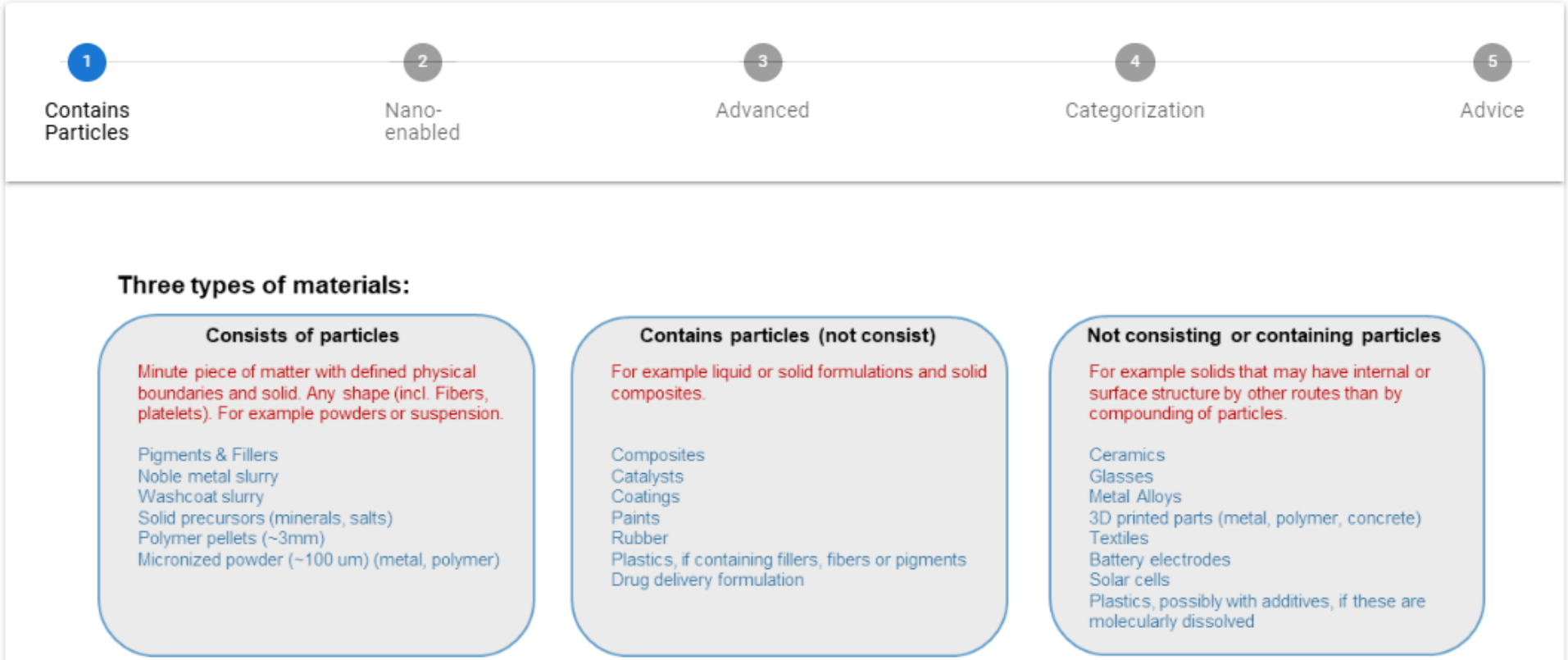
Manuscript submitted to Environmental Science: Nano; special issue on Advanced Materials

Advanced Materials Earliest Assessment (AMEA)

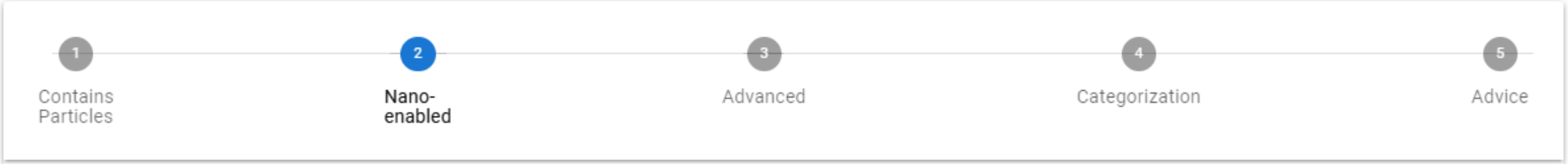
Wendel Wohlleben[1] Michael Persson[2], Blanca Suarez-Merino[3], Anders Baun[4], Veronica Di Battista[1,4], Susan Dekkers[5], Eugene P. van Someren[5], Dirk Broßell[6], Burkhard Stahlmecke[7], Martin Wiemann[8], Otmar Schmid[9], Andrea Haase[10]

[1]BASF SE, Carl-Bosch-Str. 38, 67056 Ludwigshafen, Germany
[2]Chalmers CIT, Chalmers Industriteknik, Sven Hultins Plats 1, 412 58 Göteborg, Sweden
[3]TEMAS Solutions GmbH, Lätteweg 5, 5212 Hausen, Switzerland
[4]DTU Sustain, Technical University of Denmark, Building 115, 2800 Kgs. Lyngby, Denmark
[5]TNO, Risk Analysis for Products in Development, The Netherlands
[6]Federal Institute for Occupational Safety and Health, Nöldnerstr. 40-42, 10317 Berlin, Germany
[7]Institut für Umwelt & Energie, Technik & Analytik e. V., Bliersheimer Str. 58-60, 47229 Duisburg, Germany
[8]IBE R&D Institute for Lung Health gGmbH, Münster, Germany
[9]Helmholtz Zentrum München, Ingolstädter Landstr. 1, 85764 Neuherberg, Germany
[10]German Federal Institute for Risk Assessment (BfR), Department of Chemical and Product Safety
E-mail contact: wendel.wohlleben@basf.com

AMEA questions (1/3)



AMEA questions (2/3)



Is the material nano-enabled and/or a nanomaterial in regulatory terms, or none thereof?

For **"structured materials",** ask if the structure enables the functionality. Check if the material in question is in scope of a **"regionally applicable regulatory definition"**, e.g. if the target market is in the EU, check the material against the REACH definition of a material.

Regionally applicable regulatory definition

According to Annex VI of the REACH Regulation, a **"nanoform"** is "a form of a natural or manufactured substance containing 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".

REACH

Even if the material is not in scope of the regionally applicable regulatory definition, follow ISO's definition of **"nano-enabled"**, i.e. "exhibiting function or performance only possible with **"nanotechnology"** ".

Note, that **"nanotechnology"** is defined as "application of scientific knowledge to manipulate and control matter predominantly in the **"nanoscale"** to make use of size- and structure-dependent properties and phenomena distinct from those associated with individual atoms or molecules, or extrapolation from larger sizes of the same material".

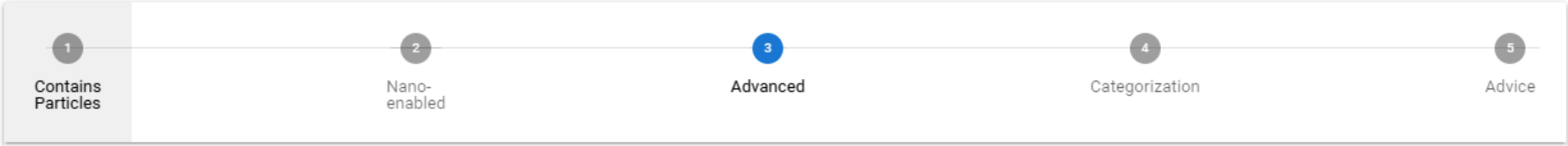
Note that a **"nanomaterial"** is defined as "a material with any external dimension in the **"nanoscale"** or having an internal structure or surface structure in the **"nanoscale"**.

While **"nanoscale"** is defined as "a length range approximately from 1 nm to 100 nm".

ISO

- (●) Yes, the materials is nano-enabled and/or in scope of the regionally applicable regulatory definition of nanomaterials
- ( ) No, the materials is not nano-enabled and not in scope of the regionally applicable regulatory definition of nanomaterials

AMEA questions (3/3)



The OECD (2022) describes AdMa as materials that are rationally designed to have

- new or enhanced properties, and/or
- targeted or enhanced structural features

with the objective to achieve specific or improved functional performance. This includes both new emerging manufactured materials, and materials that are manufactured from traditional materials. This also includes materials from innovative manufacturing processes that enable the creation of targeted structures from starting materials, such as bottom-up approaches. It is acknowledged that what are currently considered as AdMa will change with time."

OECD
new or enhanced properties
or structural features
to improve performance

In alignment with the Advanced Materials Initiative (AMI2030, cited as EMMC 2022), we refine this description and differentiate incremental innovation from AdMa. AdMa feature qualitative characteristics (Kennedy et al. 2019), specifically inherent physicochemical or biological attributes, or constitute unique combination of CoMas.

We abstain from a quantitative metric, because for some sectors of use and material categories already a 1% improvement in functional performance is a significant achievement, while in others an order of magnitude is required to disrupt the status quo. (Kennedy et al. 2019, EMMC 2022)

AMI2030
excluding incremental innovations
no quantitative metric for improved performance

To further support the assessment, AMEA proposes to consider a material as "conventional" if it can be obtained since more than a decade from several (>10) suppliers in similar quality in ton scale.

AMEA
< decade in ton scale

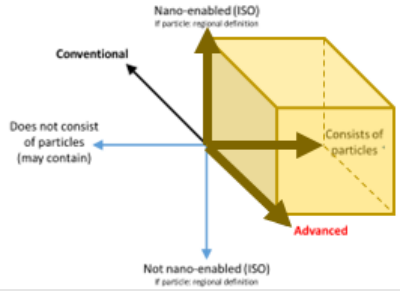
Is the manufacturing process or the material itself considered as "advanced"?

- (●) Yes
- ( ) No

AMEA results: Applicability of DSS

1 Contains Particles — 2 Nano-enabled — 3 Advanced — 4 Categorization — 5 Advice

Resulting category: *Advanced Nano-enabled Material Consisting of Particles (AdNmCp)*



- Consists of particles
- Nano-enabled
- Advanced

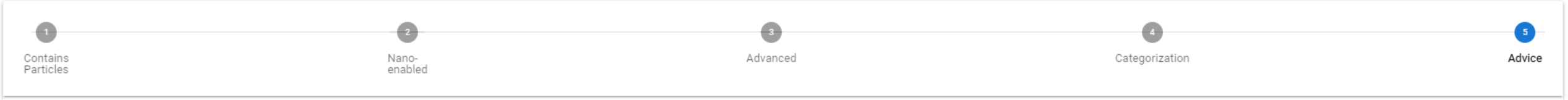
→ Consequences on applicability of HARMLESS DSS:
  → most suited for materials „consisting of particles“. Methods optimised for „nano-enabled“.
  → DSS recommends quitting if out of applicability domain.

Status wheel | Criteria checks

Ideation & Business Case Phase (A)

Harmless dss applicability	Description	Ideation & Business Case Phase (A)
Amea particlecontains	AMEA-Q1-2: If the material consists of particles (score=100) and/or is nano-enabled (score=100), the DSS is applicable and its continued use is recommended.	

AMEA results: Advice (1/5)



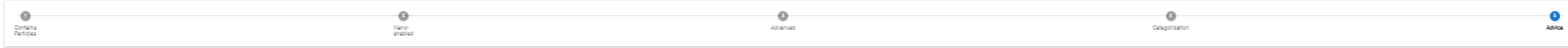
Select the innovation stage you want to get advice about

- (●) Ideation, Discovery and/or Scoping (Phase A - Stage 0-1)
- ( ) Creating a Business Case (Phase A - Stage 2)
- ( ) Lab scale (Phase B - Stage 3), also referred to as "Product Design" or "Development"

SSbD Advice for category: Advanced Nano-enabled material Consisting of Particles (AdNmCp)

and Innovation Stage: Ideation / Discovery & Scoping

AMEA results: Advice (2/5)



Select the innovation stage you want to get advice about

- (●) Ideation, Discovery and/or Scoping (Phase A - Stage 0-1)
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- ( ) Lab scale (Phase B - Stage 3), also referred to as "Product Design" or "Development"

SSbD Advice for category: Advanced Nano-enabled material Consisting of Particles (AdNmCp)
and Innovation Stage: Ideation / Discovery & Scoping

	Phase Characterization: A market need has been identified and a design is being developed for a certain P-A-R. Design principles are key to guide the innovation	**Guidance for Assessment:**
Exposure during lifecycle	Design principles focus on circularity. The intended user that is captured by the P-A-R allows a qualitative identification of hot spots, where emission into the environment and/or exposure of humans is likely. Often times, these hot spots are well known in the industry sector.	**Design Principles:** • Consider EoL design for circularity • Describe P-A-R = product, application, region (World_Business_Council_for_Sustainable_Development 2018) and qualitatively identify potential hot spots
Hazard	Design principles focus on warning signs from late lessons to early warnings: (Harremoës *et al.* 2001) (Table 2)	**Design principles from late lessons to early warnings: (Harremoës) *et al.* 2001)** • Fibers fitting the WHO criteria (HARM) • Persistancy, widespread use • Bioaccumulation, irreversible effects • Heavy metals & other GRA groups • Novelty (= trigger of AdMa discussion)
Sustainability	Design principles of the AdMa product are derived from the sustainability deficiencies of the CoMa product for the same A-R target	

Apply the universal design principles.(Subramanian et al. 2023) One of the conventional warning signs, the "novelty"(Harremoës et al. 2001) is in fact the trigger for the entire elaborate concept on AdMa that we discuss here.
If made by advanced manufacturing, consider non-chemical hazards, e.g. process-generated concerns. Examples include the intense laser radiation used in the selective laser sintering process of powder-based 3D-printing, or large-scale robots that are used for for 3D printing of concrete on construction sites.
If AdMa with multiple components (MC), transformation is a bigger issue than with single substances.(Abdolahpur Monikh et al. 2023) One should characterize the rate of release and form of release, which may not be identical to the originally synthesized material, e.g. preferential leaching from advanced composite materials, or unintentional triggering of the rare "active" AdMa.(Amorim et al. 2023) All composites are MC by definition.
If AdMa with multiple components (MC), hazards must be identified initially from the hazard of each component, even if mixture effects have to be considered at higher TRL.(Abdolahpur Monikh et al. 2023, Amorim et al. 2023) E.g. on aerogel-glassfiber-mats, one may initially screen for the hazard of the glassfiber and separately for hazard of the aerogel, where the later can be approximated by the most similar CoMa without the extreme porosity. One should, in later phases, perform hazard screenings not on the originally synthesized material but on the released entities. This was originally demonstrated on nano-composite materials.(Wohlleben et al. 2011, Saber et al. 2012, Gomez et al. 2014, Saber et al. 2016, Amorim et al. 2018) A case study is given in the AMEA paper (see introduction pages).
If AdMa, apply similarity tools & rankings to assess if AdMa versions are significantly different from each other and from CoMa. If not, the design space is less restricted in the next phase, and can be guided by performance and cost. If they are significantly different, trade-offs must be weighed, which will require dedicated tools during the lab phase, before pilot phase (to avoid investment decisions leading to failure).
If AdMa, one must provide additional controls (QA/QC) that the methods are appropriate, e.g. by using several methods with complementary measurement principles. For the prioritized endpoints, screenings tests of extrinsic properties should be compatible with or derived from guidances or test guidelines, but do not need to fulfil guideline requirements and do not need GLP status.
If nano-enabled and consisting of particles (upper right quadrant in Figure 1 and Figure 2), appropriate methods must be used for structural similarity (e.g. nanoQSARs, although these may not be fully validated), in phys-chem characterization and in the testing of extrinsic properties (e.g. screenings derived from nano-specific test guidelines,(Abdolahpur Monikh et al. 2018) IATAs for selection of most relevant properties.(Stone et al. 2020, Braakhuis et al. 2021, Murphy et al. 2021, Di Cristo et al. 2022)) Tests may, but do not need to fulfil guideline requirements, and do not need GLP status, if the GLP impacts speed and costs.
The **SSbD-DSS** supports you in the implementation of the above **AMEA** advice by guiding you through other tools, such as **WASP** and **ASDI**. If you started **AMEA** from the **SSbD-DSS**, simply press "Save & Next" and "Return to the DSS". If you started AMEA as stand-alone tool your can find the SSbD-DSS here: https://diamonds.tno.nl/harmlesspublic/decision-support-system

AMEA Results: Advice (3/5)

	Phase Characterization: A market need has been identified and a design is being developed for a certain P-A-R. Design principles are key to guide the innovation
Exposure during lifecycle	Design principles focus on circularity. The intended user that is captured by the P-A-R allows a qualitative identification of hot spots, where emission into the environment and/or exposure of humans is likely. Often times, these hot spots are well known in the industry sector.
Hazard	Design principles focus on warning signs from late lessons to early warnings: (Harremoës *et al.* 2001) (Table 2)
Sustainability	Design principles of the AdMa product are derived from the sustainability deficiencies of the CoMa product for the same A-R target

AMEA results: Advice (4/5)

	Guidance for Assessment:
Exposure during lifecycle	**Design Principles:** • Consider EoL, design for cicularity • Describe P-A-R = product, application, region (World_Business_Council_for_Sustainable_Development 2018) and qualitatively identify potential hot spots
Hazard	**Design principles from late lessons to early warnings: (Harremoës) *et al.* 2001)** • Fibers fitting the WHO criteria (HARM) • Persistancy, widespread use • Bioaccumulation, irreversible effects • Heavy metals & other GRA groups • Novelty (= trigger of AdMa discussion)
Sustainability	

AMEA results: Advice (5/5)

Apply the universal design principles.(Subramanian et al. 2023) One of the conventional warning signs, the "novelty"(Harremoës et al. 2001) is in fact the trigger for the entire elaborate concept on AdMa that we discuss here.

If made by advanced manufacturing, consider non-chemical hazards, e.g. process-generated concerns. Examples include the intense laser radiation used in the selective laser sintering process of powder-based 3D-printing, or large-scale robots that are used for for 3D printing of concrete on construction sites.

If AdMa with multiple components (MC), transformation is a bigger issue than with single substances. (Abdolapur Monikh et al. 2023) One should characterize the rate of release and form of release, which may not be identical to the original synthesized material, e.g. preferential leaching from advanced composite materials, or unintentional triggering of the rare "active" AdMa. (Amorim et al. 2023) All composites are MC by definition.

If nano-enabled and consisting of particles (upper right quadrant in Figure 1 and Figure 2), appropriate methods must be used for structural similarity (e.g. nanoQSARs, although these may not be fully validated), in phys-chem characterization and in the testing of extrinsic properties (e.g. screenings derived from nano-specific test guidelines,(Abdolahpur Monikh et al. 2018) IATAs for selection of most relevant properties.(Stone et al. 2020, Braakhuis et al. 2021, Murphy et al. 2021, Di Cristo et al. 2022)) Tests may, but do not need to fulfil guideline requirements, and do not need GLP status, if the GLP impacts speed and costs.

The **SSbD-DSS** supports you in the implementation of the above **AMEA** advice by guiding you through other tools, such as **WASP** and **ASDI**. If you started **AMEA** from the **SSbD-DSS**, simply press "Save & Next" and "Return to the DSS". If you started AMEA as stand-alone tool your can find the SSbD-DSS here: https://diamonds.tno.nl/harmlesspublic/decision-support-system

Which NAMs are used in which innovation stage

Innovation stages

Data availability

DSS Tools

NAMs

Product Idea&Screening

Gate2

Lab Scale

Gate3

Pilot scale

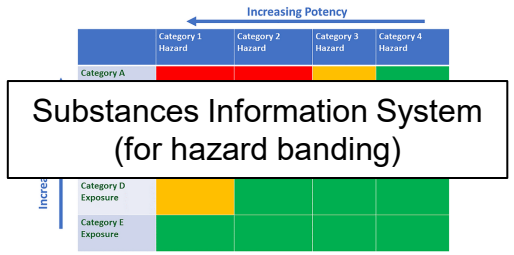
Gate4

Qualitative assessment

Quantitative assessment

WASP

14 questions based on AMEA, Stoffenmanager, NEQ, LICARA, Precautionary matrix, ...



Substances Information System (for hazard banding)

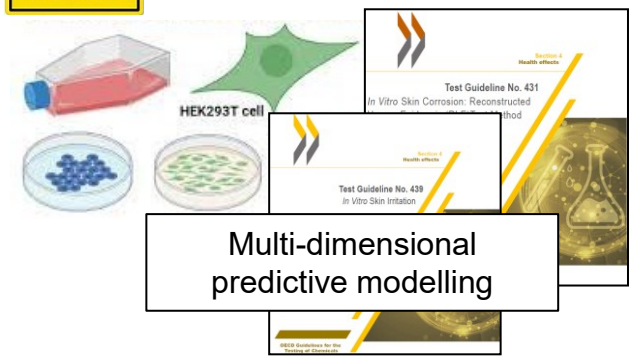
ASDI

List of descriptors based on GRACIOUS IATAs and UN SDGs

Dissolution in relevant media
Acellular (bio)reactivity

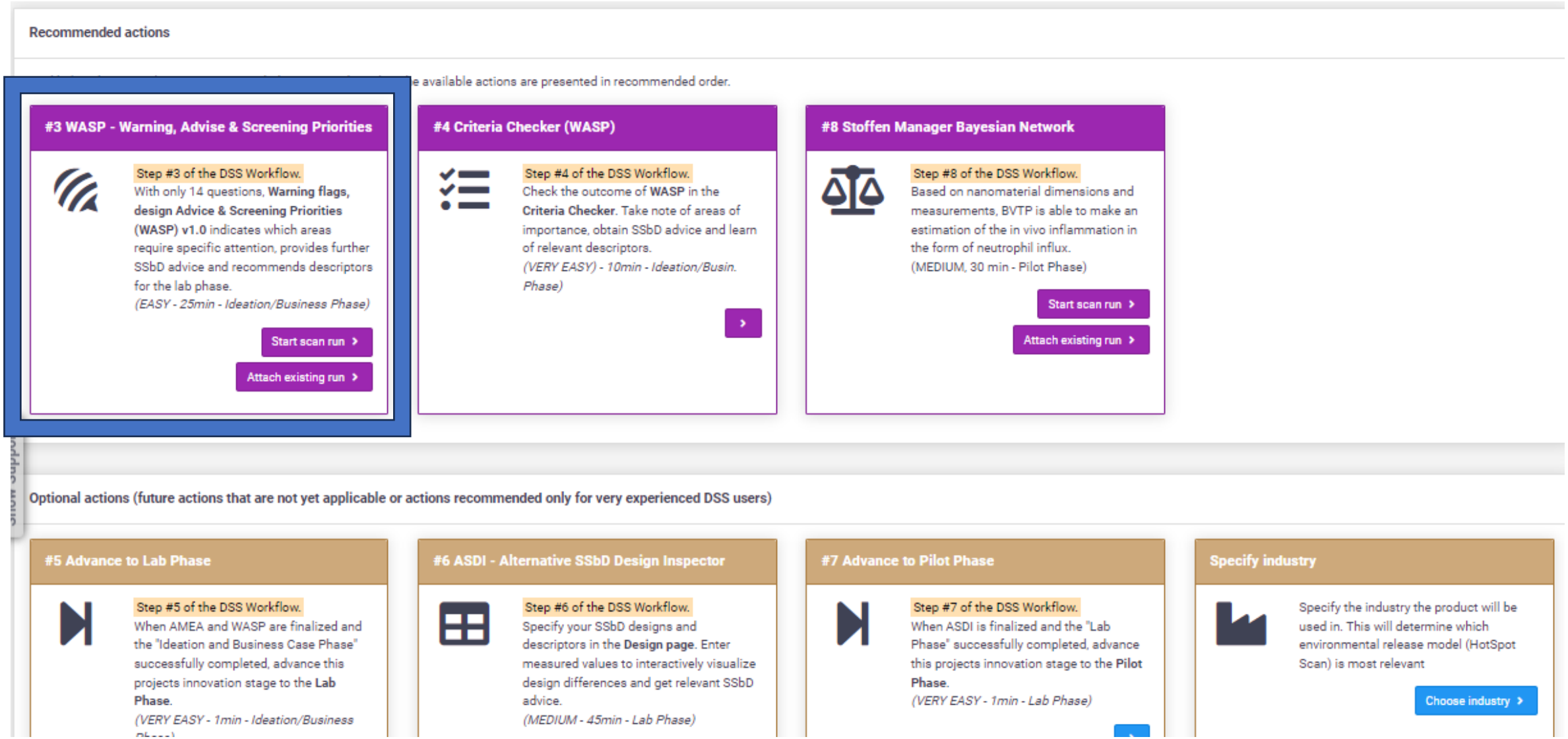
Advanced descriptors
Higher-tiered Tools

Predictive models based on physchem, in chemico and in vitro data



Multi-dimensional predictive modelling

Workflow DSS in the tool



Ideation and business case phase

Limited information available:
Raising warning flags & design and assessment advice
(qualitative assessment)

WASP: Warning flags, design Advice, Screening Priorities

14 questions in 3 sections
Safety (Exposure),
Safety (Hazard) and
Sustainability Aspects

1 Safety (Exposure) — 2 Safety (Hazard) — 3 Sustainability Aspects — 4 Early Warnings and Advice

1. Is your material in powder form or can it release dust or aerosols?

Is it possible that the material or product becomes airborn or that it releases dust that becomes airborn?

- (●) Yes
- ( ) No

2. Is consumer exposure foreseen?

Is it expected that the material will:
a) be used in a consumer product (e.g. sunscreen), or
b) be released in a such a way that consumers will be exposed (e.g. pesticide residuals on food products)?

- ( ) Yes
- (●) No

3. In which lifecycle stages is occupational exposure likely?

Production: Exposure during synthesis of the material
Manufacturing: Exposure during manufacturing of a nano-enabled product
Use (professional): Exposure during professional use of the product
End-of-Life: Exposure of workers in the waste treatment or recycling.

- [x] Production
- [x] Manufactoring
- [x] Use (professional)

WASP Results

Question	Point of attention
1. Is your material in powder form or can it release dust or aerosols?	

Advices for innovators for potential redesign	Descriptors triggered at lab phase
Answered: Yes	
Design advice: Inhalation exposure is likely. To avoid this, use liquids or dispersions. **Assessment advice:** Assess Inhalation by IATAs using Tier 1 NAMs (Braakhuis et al.,)	**GRACIOUS:** • Particle size (what they are) • Surface area (what they are) • Composition (what they are) • Dissolution (inhalation IATA) • Bioreactivity (inhalation IATA) • Inflammation (inhalation IATA) **OTHER:** • Dustiness • Respirable fraction

Reason for green/yellow light & Design advice

Assessment advice

Potential descriptors ASDI

Which NAMs are used in which innovation stage

Innovation stages

Product Idea&Screening | Gate2 | Lab Scale | Gate3 | Pilot scale | Gate4

Data availability

Qualitative assessment

Quantitative assessment

DSS Tools

WASP

14 questions based on AMEA, Stoffenmanager, NEQ, LICARA, Precautionary matrix, ...

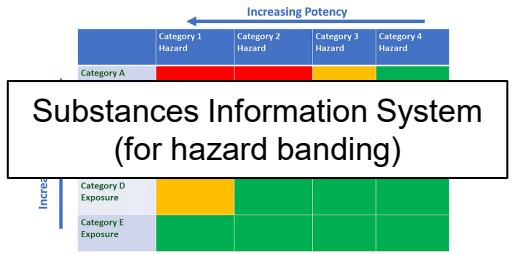
ASDI

List of descriptors based on GRACIOUS IATAs and UN SDGs

Advanced descriptors Higher-tiered Tools

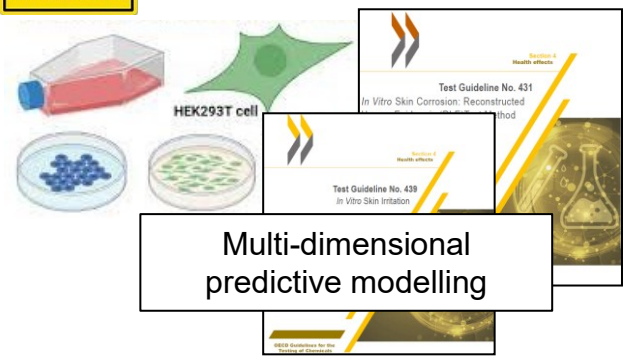
Predictive models based on physchem, in chemico and in vitro data

NAMs



Substances Information System (for hazard banding)

Dissolution in relevant media
Acellular (bio)reactivity



Multi-dimensional predictive modelling

Recommended actions

Find below the currently most recommended actions to do. Below the available actions are presented in recommended order.

#6 ASDI - Alternative SSbD Design Inspector

Step #6 of the DSS Workflow.
Specify your SSbD designs and descriptors in the **Design page**. Enter measured values to interactively visualize design differences and get relevant SSbD advice.
(MEDIUM - 45min - Lab Phase)

›

#8 Stoffen Manager Bayesian Network

Step #8 of the DSS Workflow.
Based on nanomaterial dimensions and measurements, BVTP is able to make an estimation of the in vivo inflammation in the form of neutrophil influx.
(MEDIUM, 30 min - Pilot Phase)

Start scan run ›

Attach existing run ›

Optional actions (future actions that are not yet applicable or actions recommended only for very experienced DSS users)

#7 Advance to Pilot Phase

Step #7 of the DSS Workflow.
When ASDI is finalized and the "Lab Phase" successfully completed, advance this projects innovation stage to the **Pilot Phase**.
(VERY EASY - 1min - Lab Phase)

›

Specify industry

Specify the industry the product will be used in. This will determine which environmental release model (HotSpot Scan) is most relevant

Choose industry ›

View the Status Wheel and Criteria Checker

The Status Wheel and/or Criteria Checker visualisation has been updated. Check these visualizations to gain insight in your SSbD status

View statuswheel ›

Stoffenmanager Nano hazard (SMnanoHaz)

SMnanoHaz determines a quick (Tier-1) hazard assessment based on a few questions resulting in a hazard band

Start scan run ›

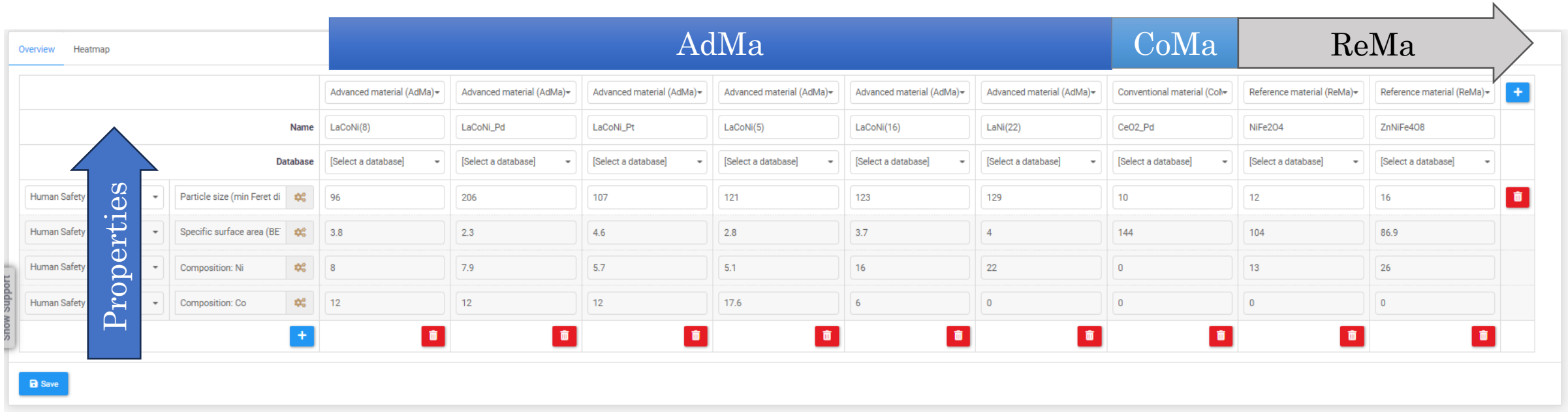
Lab phase

ASDI

Synthetised versions for screening available:
comparison of SSbD versions
(quantitative assessment)

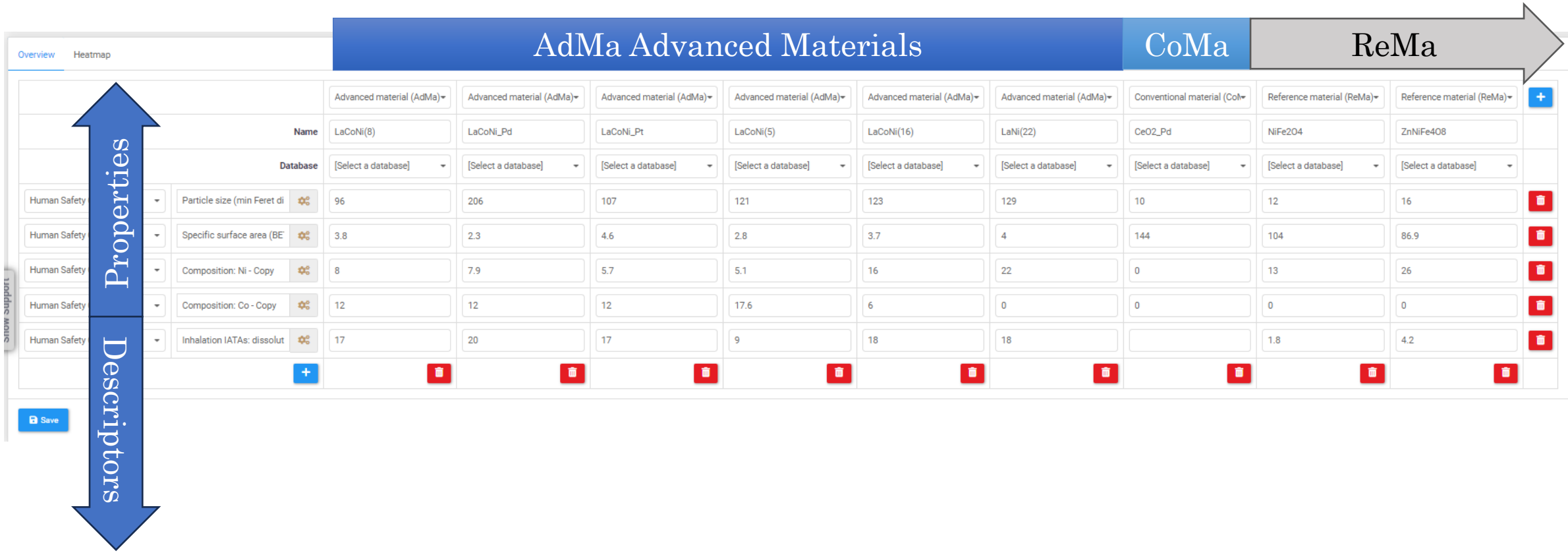
Alternative SSbD Inspector (ASDI) Matrix (1/2)

1. **Start with properties in which the SSbD versions differ (design space)**
   - Size, surface area and composition
   - For the different SSbD versions of the **Ad**vanced **Ma**terials (**AdMa**), **Co**nventional **Ma**terials (**CoMa**) and **Re**ference **Ma**terials (**ReMa**)



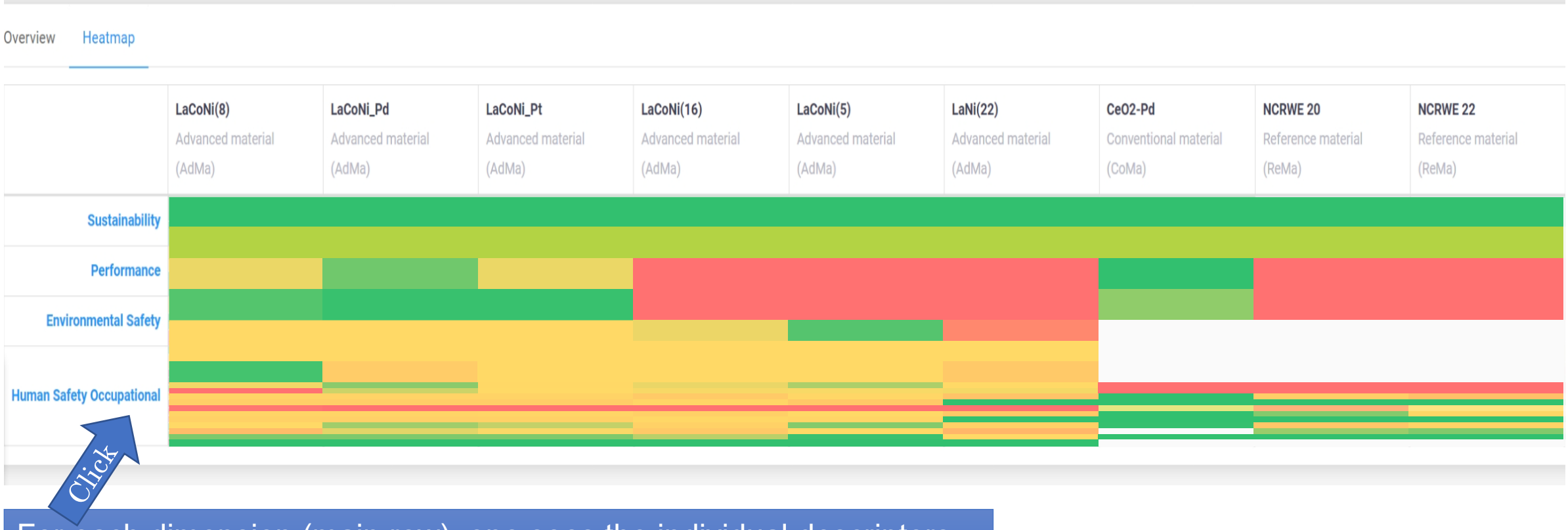
Alternative SSbD Inspector (ASDI) matrix (2/2)

2. **Select other relevant descriptors based on WASP results from ideation phase (from a default list based on the GRACIOUS IATAs & SDG target indicators)**
   - E.g. Dissolution in relevant media



		Advanced material (AdMa)	Advanced material (AdMa)	Advanced material (AdMa)	Advanced material (AdMa)	Advanced material (AdMa)	Advanced material (AdMa)	Conventional material (Col	Reference material (ReMa)	Reference material (ReMa)
	Name	LaCoNi(8)	LaCoNi_Pd	LaCoNi_Pt	LaCoNi(5)	LaCoNi(16)	LaNi(22)	CeO2_Pd	NiFe2O4	ZnNiFe4O8
	Database	[Select a database]	[Select a database]	[Select a database]	[Select a database]	[Select a database]	[Select a database]	[Select a database]	[Select a database]	[Select a database]
Human Safety	Particle size (min Feret di	96	206	107	121	123	129	10	12	16
Human Safety	Specific surface area (BE	3.8	2.3	4.6	2.8	3.7	4	144	104	86.9
Human Safety	Composition: Ni - Copy	8	7.9	5.7	5.1	16	22	0	13	26
Human Safety	Composition: Co - Copy	12	12	12	17.6	6	0	0	0	0
Human Safety	Inhalation IATAs: dissolut	17	20	17	9	18	18		1.8	4.2

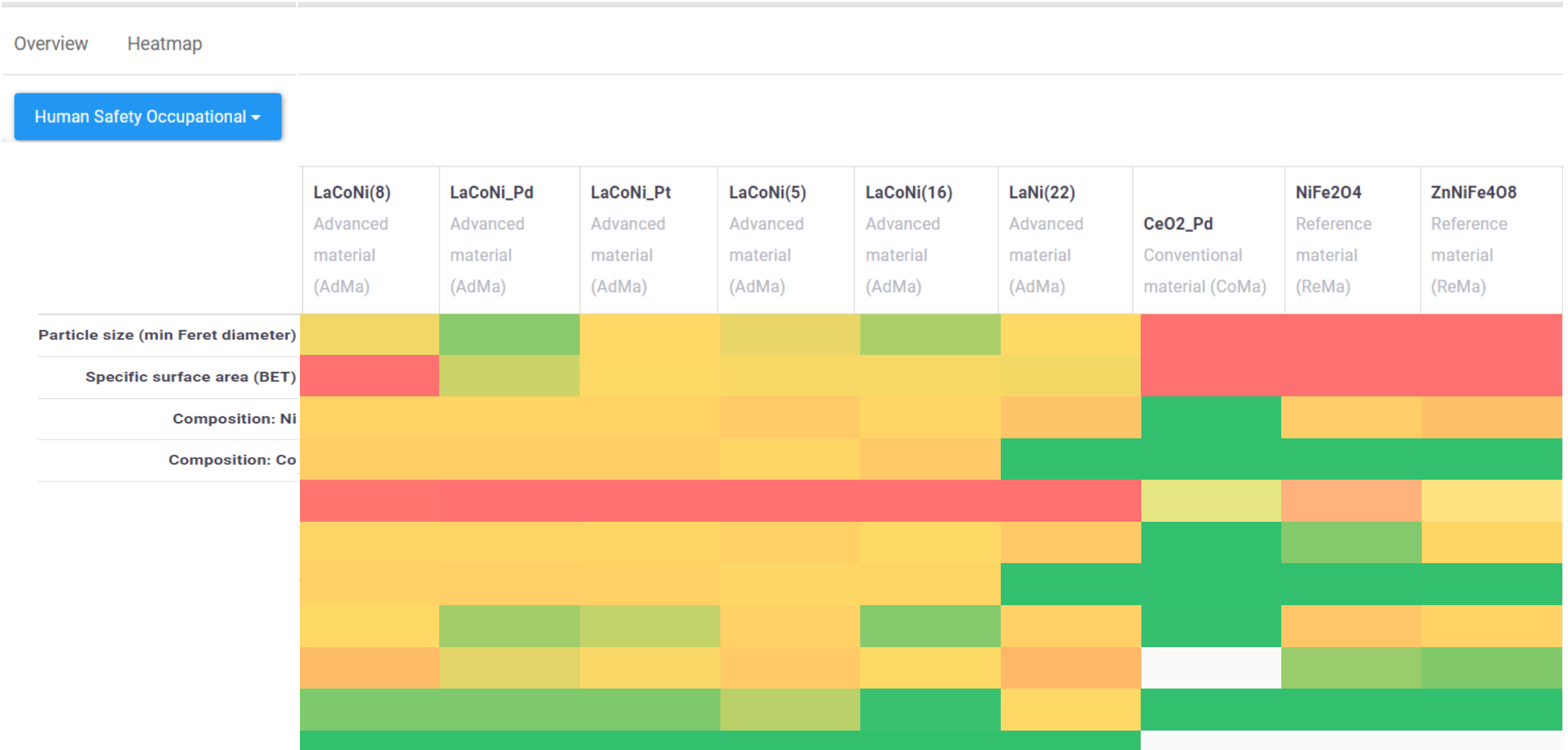
Alternative SSbD Inspector (ASDI) results



For each dimension (main row), one sees the individual descriptors (small row) and their color-coded values.

Rather than a forced color, we believe showing the individual results provides more insight into the coherence within a dimension

Alternative SSbD Inspector (ASDI) results



Alternative SSbD Inspector (ASDI) results

Overall assessment

1. Check for significant differences between SSbD versions
2. Consider correlation to design space (→ re-design advice)

Evaluation

1. Limited differences *between* the perovskites SSbD versions. More differences are observed for entire perovskite *family vs. reference* materials (NRCWE)
2. Increased Nickel content correlates with increased hazard potency, doping with Palladium tends to decrease potency & increase performance

Suggested SSbD decision: LaCoNi_Pd, but re-design to lower Ni content.

Which NAMs are used in which innovation stage

Innovation stages

Product Idea&Screening

Gate2

Lab Scale

Gat 3

Pilot scale

Ga e4

Data availability

Qualitative assessment

Quantitative assessmen

DSS Tools

WASP

14 questions based on AMEA, Stoffenmanager, NEQ, LICARA, Precautionary matrix, ...

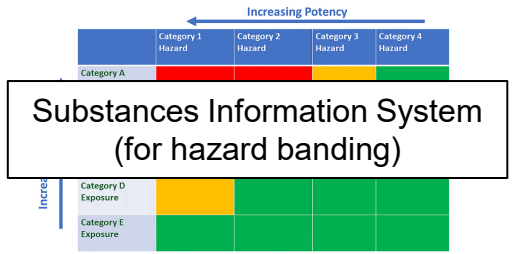
ASDI

List of descriptors based on GRACIOUS IATAs and UN SDGs

Advanced descriptors Higher-tiered Tools

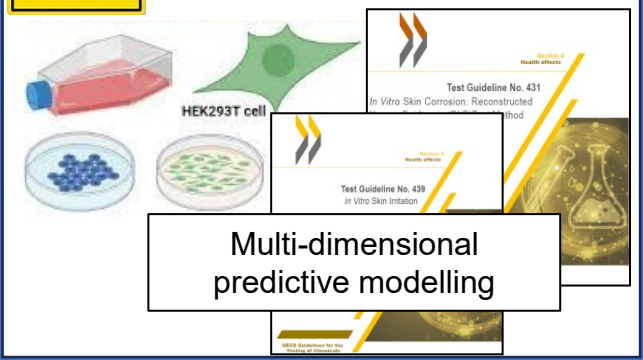
Predictive models based on physchem, in chemico and in vitro data

NAMs



Substances Information System (for hazard banding)

Dissolution in relevant media
Acellular (bio)reactivity



Multi-dimensional predictive modelling

Pilot phase

Production scale up:
assess one SSbD version
(quantitative assessment)

Recommended actions

Find below the currently most recommended actions to do. Below the available actions are presented in recommended order.

#8 Stoffen Manager Bayesian Network

Step #8 of the DSS Workflow.
Based on nanomaterial dimensions and measurements, BVTP is able to make an estimation of the in vivo inflammation in the form of neutrophil influx.
(MEDIUM, 30 min - Pilot Phase)

Attach existing run › | Start scan run ›

Optional actions (future actions that are not yet applicable or actions recommended only for very experienced DSS users)

Specify industry

Specify the industry the product will be used in. This will determine which environmental release model (HotSpot Scan) is most relevant

Choose industry ›

View the Status Wheel and Criteria Checker

The Status Wheel and/or Criteria Checker visualisation has been updated. Check these visualizations to gain insight in your SSbD status

View statuswheel ›

Stoffenmanager Nano hazard (SMnanoHaz)

SMnanoHaz determines a quick (Tier-1) hazard assessment based on a few questions resulting in a hazard band

Start scan run ›

Pilot phase (under development)

Safety

- more complex models and in vitro tests, quantitative predictive exposure and hazard models.

Sustainability

- (semi)quantitative SDG target indicators

Visualisation in status wheel

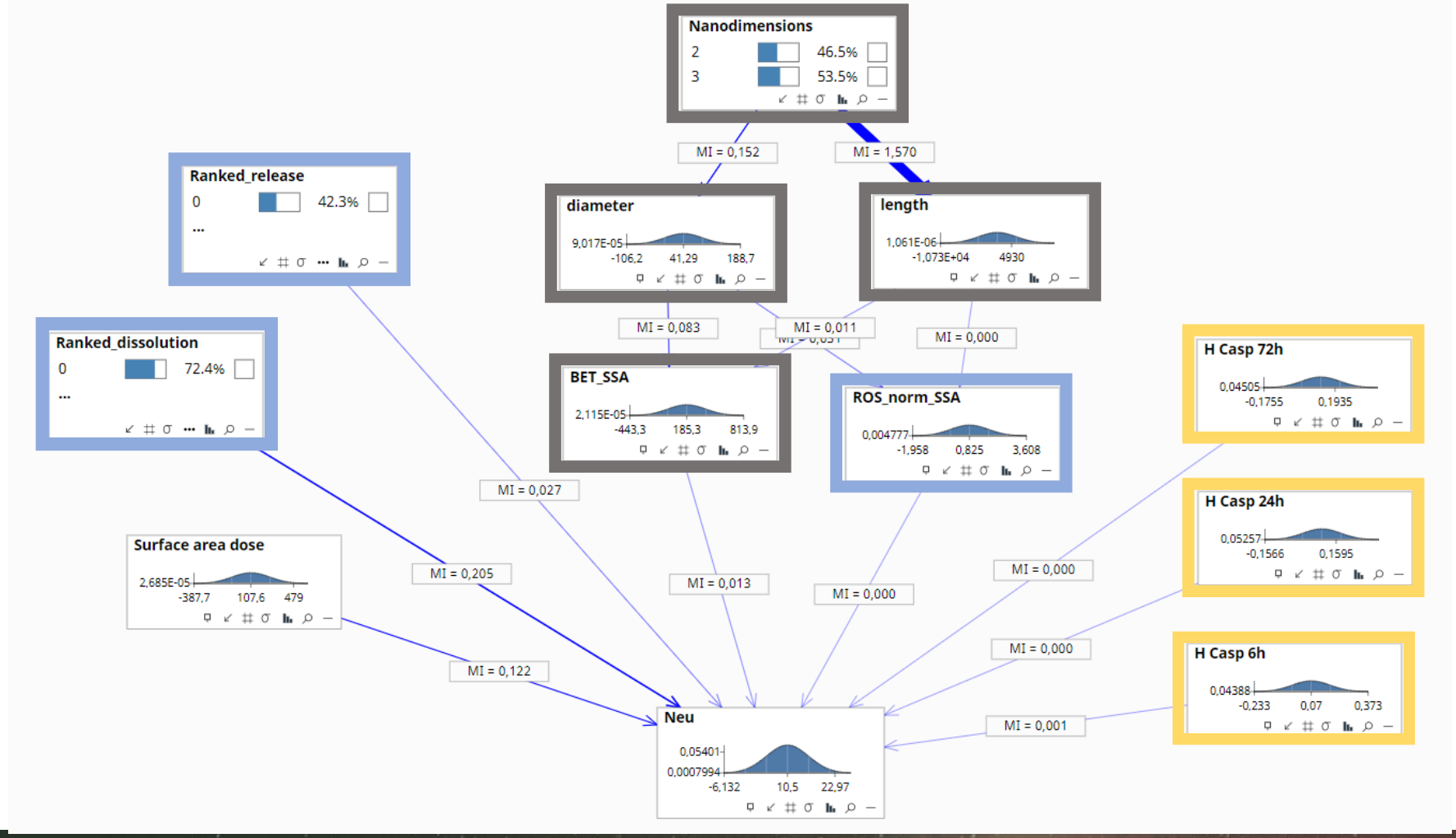
- Normalized scores for each SSbD aspect
- Including uncertainty (range)

** Fully traceable where value is based on (when click)*

Existing methods and tools that may be included in the pilot phase

- **Human en environmental exposure models**
- **Release testing**
- **In vitro toxicity testing**
- **In vivo ecotoxicity testing**
- **Predictive hazard modelling**
  - Using AOP and in vivo anchoring
  - E.g. predictive neutrophil influx (common critical effect in vivo inhalation studies)
    - Using physicochemical, in chemico and/or in vitro data
    - Several models are developed using different statistical, ML and AI methods

Example of a predictive model:
Bayesian Network model to predict neutrophil influx



Physicochemical

In chemico

In vitro
(not necessary)

Comparison of different predictive models

The best performing models per category (statistical and/or ML method) are highlighted

Variable Set Name:	**Phys-Chem + in chemico + in vivo (SAD)**					**Phys-Chem + in chemico + in vitro CASP H (all time points) + in vivo (SAD)**				
Variables:	['SAD', '**Neu**', 'diameter', 'length', 'BET_SSA', 'Nanodimensions', 'ROS_norm_SSA', 'Ranked_dissolution', 'Ranked_release']					['SAD', '**Neu**', 'diameter', 'length', 'BET_SSA', 'Nanodimensions', 'ROS_norm_SSA', 'Ranked_dissolution', 'Ranked_release', 'H Casp 6h', 'H Casp 24h', 'H Casp 72h']				
	MAE	**MSE**	**RMSE**	**RMSLE**	**R2**	**MAE**	**MSE**	**RMSE**	**RMSLE**	**R2**
Linear Regression	1.04	1.81	1.35	0.13	0.37	1.01	1.69	1.3	0.13	0.41
Ridge Regression	1.04	1.81	1.35	0.13	0.37	1.01	1.7	1.3	0.13	0.41
Lasso Regression	1.43	2.89	1.7	0.17	-0.0	1.43	2.89	1.7	0.17	-0.0
Decision Tree Regression	**0.62**	**0.62**	**0.79**	**0.08**	**0.79**	**0.62**	**0.62**	**0.79**	**0.08**	**0.79**
Random Forest	**0.62**	**0.62**	**0.79**	**0.08**	0.78	**0.62**	**0.62**	0.79	**0.08**	0.78
KNN Model	**0.62**	0.63	0.8	**0.08**	0.78	0.65	0.71	0.84	0.09	0.75
Support Vector Machines (SVM)	1.06	1.91	1.38	0.14	0.34	1.03	1.8	1.34	0.14	0.37
Neural Network Regression	0.75	0.9	0.95	0.1	0.69	0.68	0.79	0.89	0.09	0.73
Bayesian Network SL	1.1	1.98	1.41	0.14	0.31	1.09	1.95	1.4	0.14	0.32
Bayesian Network manual A)	0.85	1.16	1.08	0.11	0.6	0.79	1.06	1.03	0.11	0.63
Bayesian Network manual B)	1.13	2.01	1.42	0.14	0.3	1.13	1.99	1.41	0.14	0.31

1 Nanomaterial Dimensions

2 Nanomaterial Measurements

3 Tox5 Measurements

What is the diameter (on average) in nanometres of the nanomaterial? Diameter

Please provide an estimate of the average diameter of the nanomaterial in nanometres [nm] as an integer within a range between 1 [nm] and 225 [nm].

206

What is the length (on average) in nanometres of the nanomaterial? Length

Please provide an estimate of the average length of the nanomaterial in nanometres [nm] as an integer within a range between 10 [nm] and 17500 [nm].

What is the length (on average) in nanometres of the nanomaterial?

What is the Specific Surface Area (in square metre per gram) of the nanomaterial? Specific Surface Area

Provide an estimate of the Specific Surface Area (SSA) of the nanomaterial in square metre per gram [m^2/g] as a decimal within a range between 2.74 [m^2/g] and 1142 [m^2/g]. The specific surface area is normally obtained using the Brunaer-Emmett-Teller (BET) gas adsorption method.

2.3

What is the morphology of the nanomaterial? Shape

Select either Sheet or Elongated. (note: this tool is not applicable for spherical morphology due to limited training data)

- (●) Spherical
- ( ) Elongated

1 Nanomaterial Dimensions

2 Nanomaterial Measurements

3 Tox5 Measurements

What is the Reactive Oxygen Species production?

ROS production (ecellular)

Please provide an estimate of the Reactive Oxygen Species production (ROS) as a decimal ROS SSA normalized to carbon black (Printext90) within a range between 0.000123035 and 4.593511525.

0.27

What is the (binned) Dissolution Rate of the core nanomaterial?

Dissolution rate

Please select one of the bins below that match the value of the estimated average Dissolution Rate in [ng/cm^{2}m/h].

- ○ x <= 0.01 [ng/cm2/h]
- ◉ 0.01 < x <= 0.1 [ng/cm2/h]
- ○ 0.1 < x <= 1.0 [ng/cm2/h] [NM-110]

What is the (binned) Release of toxic metals (after 1 day) of the nanomaterial?

Release of toxic metals

Please select one of the bins below that match the value of the estimated average Release of toxic metals after 1 day in milligram per liter [mg/L].

- ○ x <= 0.001 [mg/L]
- ◉ 0.01 < x <= 0.1 [mg/L]
- ○ 0.1 < x <= 1 [mg/L]
- ○ 1 < x <= 10 [mg/L]

1 Nanomaterial Dimensions

2 Nanomaterial Measurements

3 Tox5 Measurements

What is the ToxScore for HepG2 cells, at the 6h time point, for the specific Caspase endpoint?

In vitro caspase assay HebG2 cells 6h

Please provide the ToxScore obtained from HepG2 cells harvested after 6 hours [h] for the specific Caspase endpoint in micrometer per milliliter [ug/ml] as a decimal within a range between

0.03

What is the ToxScore for HepG2 cells, at the 24h time point, for the specific Caspase endpoint?

In vitro caspase assay HebG2 cells 24h

Please provide the ToxScore obtained from HepG2 cells harvested after 24 hours [h] for the specific Caspase endpoint in micrometer per milliliter [ug/ml] as a decimal within a range between

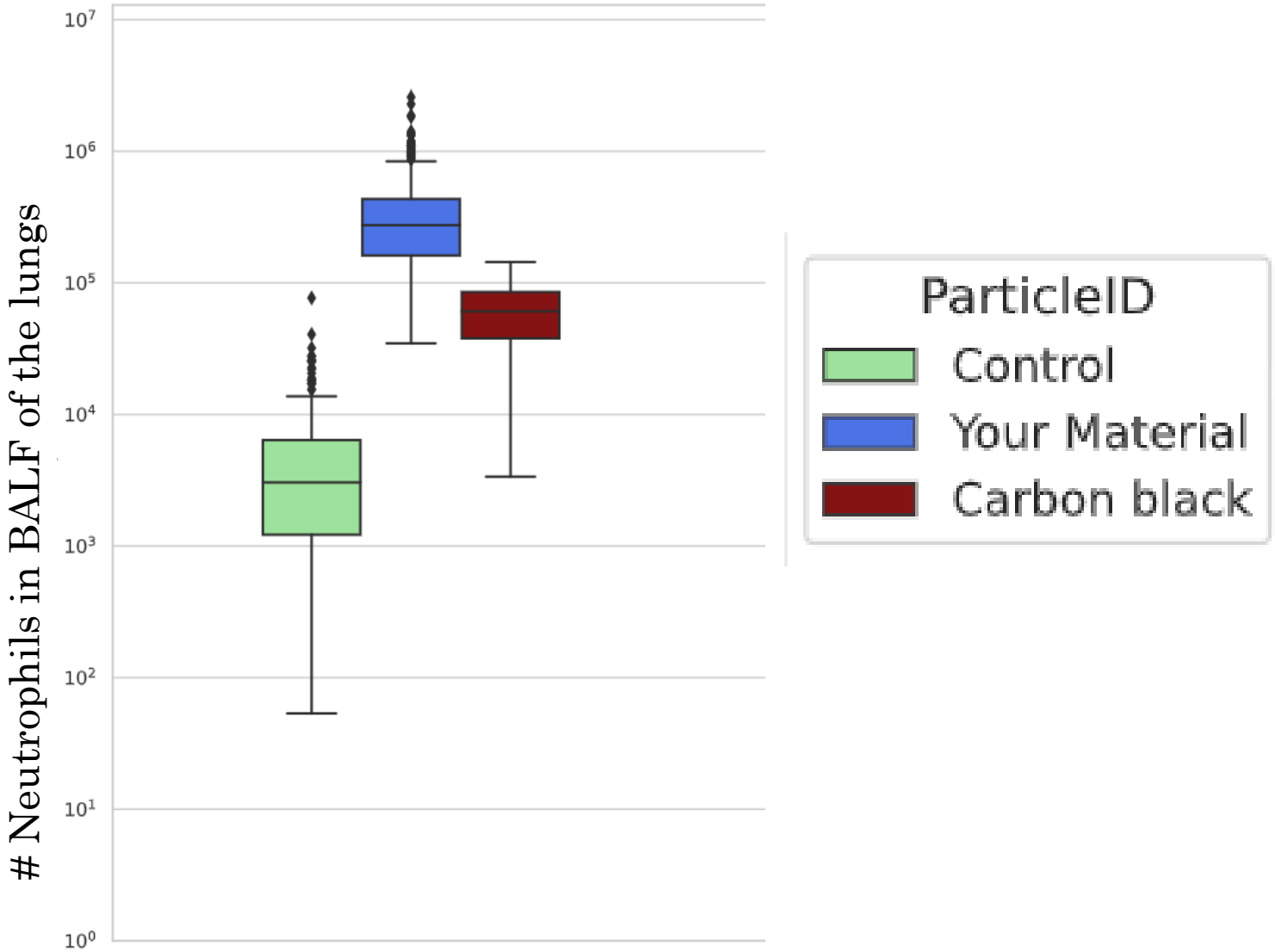
0.05

What is the ToxScore for HepG2 cells, at the 72h time point, for the specific Caspase endpoint?

In vitro caspase assay HebG2 cells 72h

Please provide the ToxScore obtained from HepG2 cells harvested after 72 hours [h] for the specific Caspase endpoint in micrometer per milliliter [ug/ml] as a decimal within a range between

0.27


Neutrophils in BALF of the lungs
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
ParticleID
Control
Your Material
Carbon black

HARMLESS

Q & A - Discussion - Get involved

Applicability of user-friendly HARMLESS Decision Support System for Safe(r)-and- Sustainable(r)-by-Design (SSbD) AdMa-enabled Product Development

Otmar Schmid (HMGU)

HARMLESS

Interactive Q&A Session (part 1)

Questions and Discussion on what is presented so far

Otmar Schmid (HMGU)

HOUSEKEEPING RULES

Thank you for accepting these rules that shall ensure a smooth running of the workshop!

- Please use a headset and mute your microphone if you are not speaking.
- Please deactivate your camera if you are not talking.
- Questions
  - Please raise your hand if you want to say something.
  - OR use Chat: Start with typing “?”.
    Based on the entries in the chat the moderator will pick up questions for further discussion within the group.

HARMLESS

Interactive Q&A Session (part 2)

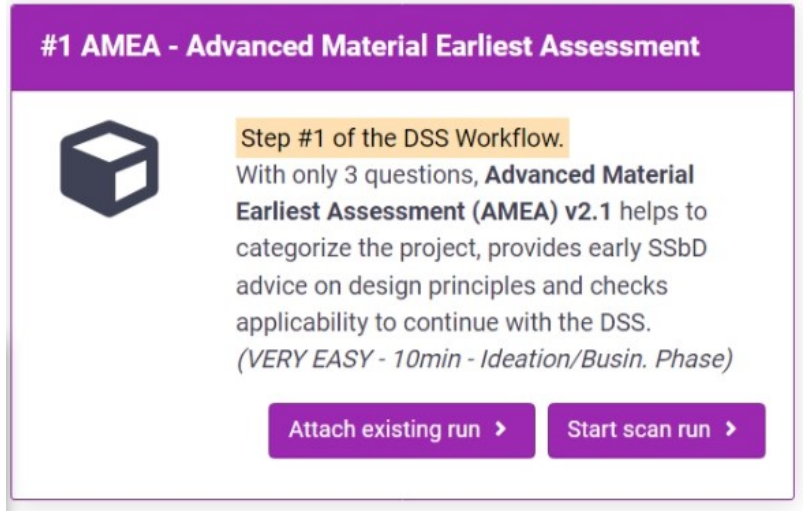
Plenary Filling in of AMEA with all participants using case suggested from workshop participants

Otmar Schmid (HMGU)

Fill in AMEA 2.1 together

We have seen AMEA for the perovskite use case …

Who wants to present their case to plenary fill in AMEA? (only three questions)



Three questions:

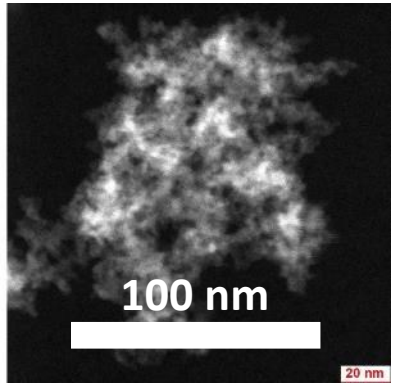
1. Does it contain/consist of particles?
2. Is it nano-enabled?
3. Is it considered advanced?

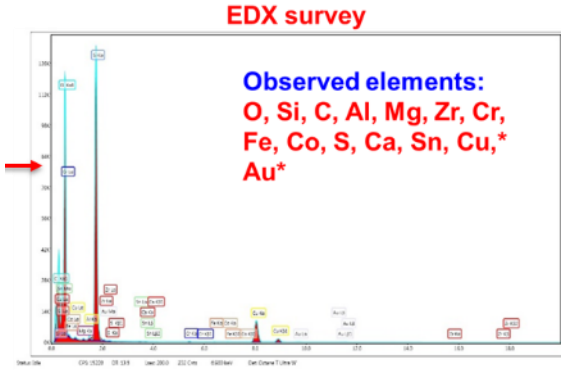
AMEA Category & Early Advice on design principles and continue with SSbD-DSS?

Fibre-aerogel-mats for façade insulation

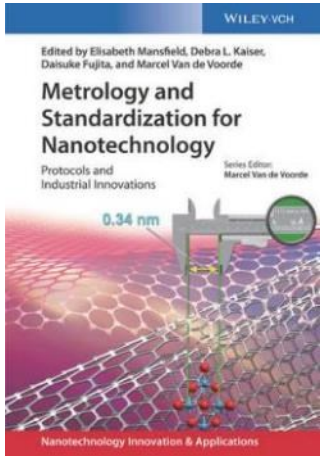
Case Study 4

- **SbD concern**
  - High internal porosity of aerogel, if fragmented
  - Fibre fragments, organic modifications
- **SbD design space**
  - Composition, choice of fibre support, organic modification, optionally inorganic coatings to protect against mechanical stresses.
- **Intended functionality**
  - Thermal insulation with record effectiveness at low thickness, e.g. around windows, campers, …
- **Conventional alternative**
  - Mineral wool mats (3 times thicker →)
  - Polymer foams panels





Singh et al (2021) J. Haz. Mater. 422: 126771



Wohlleben et al (2017) ed. Mansfield, DOI 10.1002/9783527800308.ch25

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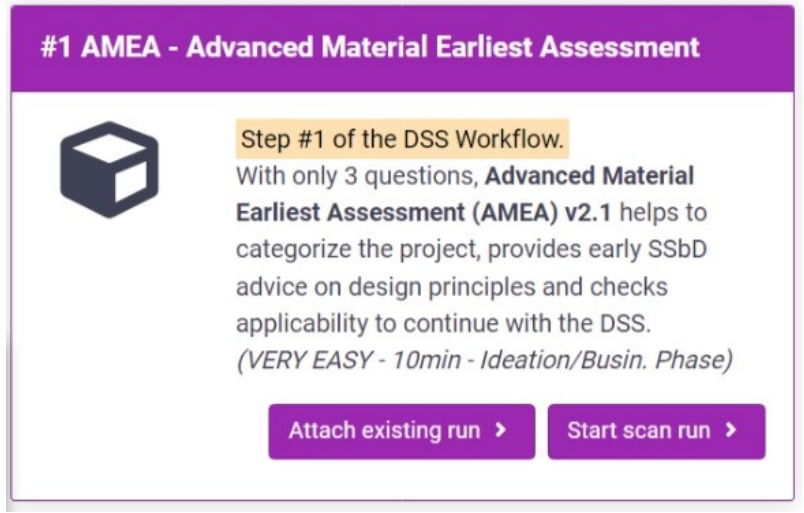
Interactive Q&A Session (part 3)

Access to AMEA for workshop participants

Otmar Schmid (HMGU)

Today's AMEA 2.1 sneak-peak



Use this short URL to jump directly into AMEA 2.1 without registration etc.

https://bit.ly/harmless-demo

Will paste this URL also in the chat!

The AMEA Demo is not designed for telephone screens!
Only for wide-screen devices (laptop, pc, tablets)

Three questions:

1. Does it contain/consist of particles?
2. Is it nano-enabled?
3. Is it considered advanced?

Who wants to present their case to plenary fill in AMEA?

AMEA Category & Early Advice on design principles and continue with SSbD-DSS?

HARMLESS

Webinar Wrap-up

Otmar Schmid (HMGU)

Webinar Wrap-up

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- **Consultancies** - Become a “BETA” tester for the HARMLESS DSS
- **SMEs** – learn if/how the HARMLESS DSS /eNanoMapper DB/tools can help you

FOLLOW US TO NEVER MISS A THING!

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