ACEnano

Analytical and Characterisation Excellence

Analytical and Characterisation Excellence in nanomaterial risk assessment: A tiered approach

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Summary

The ACEnano project is working towards developing a widely implementable and robust tiered approach to nanomaterial physicochemical characterisation that aims to simplify and facilitate the hazard and exposure description of these materials and its transcription into a reliable nanomaterials grouping framework. To support these goals, a dedicated Knowledge Infrastructure was developed. The physicochemical characterisation methods for nanomaterials developed, optimised and standardised during ACEnano have been specifically selected to be used in nanomaterial risk assessment. Therefore, the produced data always has to be viewed in this setting and interplay with other data resources with hazard, exposure and fate data as organised e.g by the NanoCommons project. Importantly, these links have also to be manifested in the ontologies used, because they provide the semantic model to allow searching across different sources and allow combining and enriching data. In this context of information science, the ontologies are defined as controlled terminologies used in a domain together with an explicit representation of the relationships between different entities. Ontologies thus provide an effective means for the standardisation and integration, as well as the flexible scientific analysis of data.

Several EU or international projects in the area of nanosafety are addressing issues related to the nanomaterials ontology and work towards harmonising terminologies and make them interoperable. In ACEnano, WP4 is covering this area within the project and also externally, by establishing collaborations and joint activities (e.g. training events and hackathons) with other projects. In brief, the goal of the ACEnano ontology is to strengthen the physicochemical characterisation area in existing nanomaterial safety ontologies and, in this way, provide the controlled terminology required for the data annotation and analysis pipelines generated and produced in the other work packages and later across the complete nanosafety community.

This report demonstrates how ACEnano has contributed to creating a harmonised nanomaterials ontology by covering the specific requirements of methodological advances in nanomaterial characterisation, improved analytical setups, and refined physicochemical characteristics. This was achieved within ACEnano and beyond and the causal relationship of nanomaterial measurands to fate, exposure, hazard and, finally, risk and safety was established. This resulted in the release of the first version of the physicochemical methodology part of the nanomaterial ontology, which is now being integrated into eNanoMapper and thus made available to the wider scientific community using this repository.

1. Introduction

Ontology translates into"study of being" combining the greek word ὄ ν τ ο ς = "being; that which is" with λ ο γ ί α = "discussion; logical discourse". From its starting point as a philosophical studies concept that directly relates to being, the term ontology is now more broadly used as a (partial) specification of a shared conceptualisation, i.e., it is usually a logical theory that expresses the conceptualisation explicitly in some language. A conceptualisation can be defined as an intensional semantic structure that encodes implicit knowledge constraining the structure of a piece of a domain.

In computer science and information science, an ontology encompasses a representation, formal naming and definition of the categories, properties and relations between the concepts, data and entities that substantiate one, many or all domains of discourse [1]. In this way, an ontology is formally a data model that represents a domain or multiple domains and is used to reason about the objects in that domain and the relations between them. In other words, ***ontologies are controlled vocabularies of terminology used in a domain together with an explicit representation of the relationships between different entities. Ontologies thus provide an effective means for the standardisation and integration, as well as the flexible scientific analysis of data***. Explicit formal relationships between entities support advanced automated reasoning for inference and error detection.

The use of ontologies began in the biological sciences as the first natural science community around 1998 with the development of the Gene Ontology (GO). By 2007, there was sufficient interest and activity in the area to merit national and international coordination efforts such as the Open Biomedical Ontologies (OBO) Foundry or the National Center for Biomedical Ontologies. The nanosafety community acknowledged the importance of using ontologies almost immediately after its establishment as a measure to foster safe and sustainable nanomaterials and nanotechnology innovations. Ontologies allowed knowledge and data exchange between all the different disciplines involved in the development of nanomaterial risk assessment approaches. These disciplines reach from physical-chemical characterisation, hazard estimation to fate and exposure studies in very complex systems. Projects like eNanoMapper[1] devoted a large part of their activities to the development of a nanosafety or more general nanomaterial (NM) ontology [2] and many former and current Horizon 2020 projects have dedicated work packages for ontology development. These projects have each concentrated on specific areas of the nanomaterial domain. To guarantee interoperability and harmonize the terminology coming from these different projects and avoid repetition of work, the EU NanoSafety Cluster (NSC) especially through its Working Group F[2] is coordinating these different activities. One area identified where existing ontologies as well as data infrastructures are not (yet) fully developed is the physicochemical characterisation of nanomaterials. The existing terminology added e.g., to the eNanoMapper ontology appeared not sufficient or not flexible enough to represent the causal relationships between nanomaterial (NM) property measurands and their fate, exposure and hazard during risk assessment.

WP4 in ACEnano is designed to overcome these limitations and, at the same time, guarantee

[1] http://www.enanomapper.net/
[2] https://www.nanosafetycluster.eu/nsc-overview/nsc-structure/working-groups/wgf/

the alignment of the work with other European and international initiatives such as eNanoMapper as the central ontology and database for projects of the NanoSafety Cluster, NANoREG, Nano Exposure and Contextual Information Database (NECID), the Center for the Environmental Implications of Nanotechnology, and the EU-US CoR activities.

Here, we report how ACEnano has contributed to creating a harmonised NM ontology by covering the specific requirements of methodological advances in NM characterisation, improved analytical setups, refined physicochemical characteristics, within ACEnano and beyond and the causal relationship of their measurands to fate, exposure, hazard and, finally, risk and safety. This resulted in the release of the first version of the physicochemical methodology part of the nanomaterial ontology, which is now being integrated into eNanoMapper.

1.1 Nanomaterial and nanosafety ontologies

Semantic annotation using defined terminology and ontologies has been identified as a prerequisite for efficiently sharing and reusing all existing nanosafety related data. This is due to the fact that many different types of data from physico-chemical characterization, hazard, exposure and fate have to be integrated into the risk and safety assessment and this data cannot be managed in a single data warehouse but should be made available in different databases optimized for the specific type of data. The ACEnano protocols and data warehouse fulfills this requirement for physico-chemical data and is now being integrated with databases optimized for the other areas based on the NanoCommons concepts. Therefore, also the ontology used in ACEnano has to be accepted and re-used far beyond the ACEnano project itself. This is achieved by aligning the Acenano ontology with new developments within the major ontology activities in Europe and world-wide. Three of these are most relevant and will be shortly introduced here:

1. As already mentioned, the eNanoMapper first developed in the project with the same name and now continued by NanoCommons has been selected as the central ontology for projects of the EU NanoSafety Cluster. It aims to cover the full scope of terminology needed to support research into nanomaterial safety especially for aggregation of data and knowledge across European and international research efforts in the nanosafety domain. It builds and reuses terminology from multiple pre-existing external ontologies such as the NanoParticle Ontology, Ontology of Adverse Events, Experimental Factor Ontology, Ontology for Biomedical Investigations, BioAssay Ontology, Environment Ontology and more, in this way combining concepts and classes from the nanomaterial sector, biological and to a lesser extend physico-chemical experimentation, health, adversity as well as environmental aspects. The last major release (https://doi.org/10.5281/zenodo.3382100) was made public on August 30 2019 and is available e.g. at NCBO Bioportal[3] (see **Figure 1**) and includes 12,732 terms.

[3] https://bioportal.bioontology.org/ontologies/ENM

Because of its general purpose as an ontology for nanosafety, eNanoMapper has been used as the starting point for the development of more focused aspects for nanosafety by other projects. Examples are the US-based NanoInformatics Knowledge Commons (NIKC) looking at exposure and fate scenarios, the GRACIOUS project focusing on read-across and grouping and finally, ACEnano, as described in more detail below. All these projects are committed to integrating results back to the eNanoMapper ontology. To show the engagement and the full commitment for the adoption of the eNanoMapper ontology concepts, ACEnano is now also listed on the BioPortal website as supporting project.

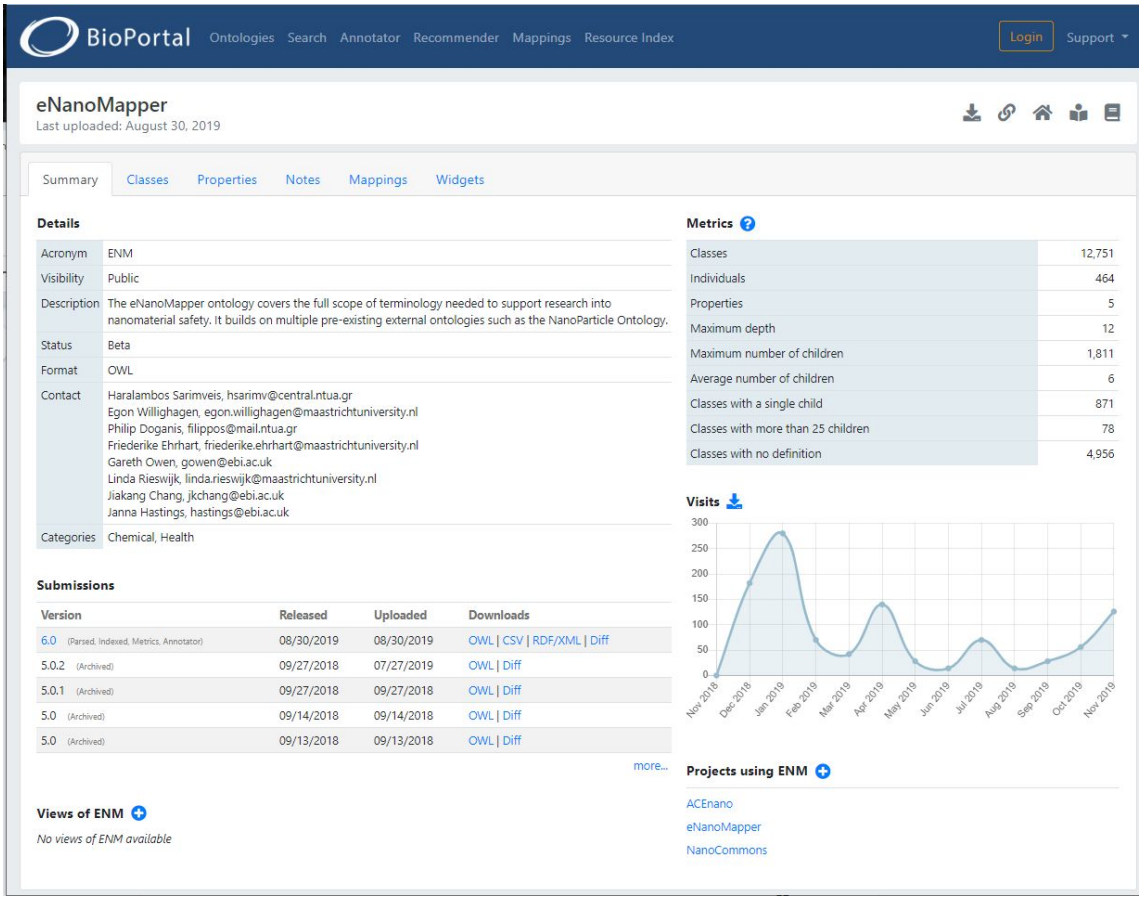

Figure 1. The eNanoMapper ontology on the NCBO Bioportal

2. The eTOX project (2010-2016) funded under the Innovative Medicines Initiative (IMI) was a collaboration between 13 pharma companies, 11 academia institutions and 6 SMEs. It accomplished an effective synergic sharing of historical toxicological data within the pharmaceutical industry via the eTOXsys platform developed in the project. To facilitate the harmonization of the data coming from all these different companies, a large part of the project was devoted to the development of the eTOX ontology. Even if the use case was for small, pharmaceutical-relevant molecules, the coverage of medical and biological experimentation is relevant for the nanosafety area and ACEnano. Unfortunately, the eTOX ontology is not yet made available to ontology portals and lookup services such as BioPortal and the Ontology Lookup service described above and, thus, combined usage with other ontologies like eNanoMapper

or even the re-usage of terminology is not directly possible.

3. While eTox could be used to strengthen the eNanoMapper ontology with respect to important parts in the medicinal, biological area, the European Materials Modelling Ontology (EMMO)[4] could play a similar role with respect to nanomaterial characterisation and *in silico* methods therein. The objective of EMMO has been defined as becoming a practical tool to achieve interoperability in the areas of describing, processing, characterizing and modelling of materials and of their properties. EMMO also aims to provide formal categorization schemes to complement machine learning, to facilitate digitalization of industrial materials technologies, and to help with the integration of artificial intelligence (AI) and Big Data approaches. Since the EMMO ontology is still under development and only available as a pre-release, interoperability with eNanoMapper has still to be proven. It is also important to mention that the ontology has a strong physics focus with an ontological framework built around concepts like elementary particles, wave-particle dualism, finiteness of space and time intervals coming from the perspective for experimental physics. This might lead to conflicts in the definition of specific terms used in different contexts in the physics and the nanosafety domain, where the latter is more dominated by toxicologists, biologists and chemists.

1.2 ACEnano protocols and data context

The ACEnano project is working towards developing a widely implementable and robust tiered approach to nanomaterials physicochemical characterisation that will simplify and facilitate contextual (hazard or exposure) description and its transcription into a reliable nanomaterials grouping framework. To support these goals, a dedicated Knowledge Infrastructure[5] was developed. The online platform facilitates the access and sharing of methodology applied in nanosafety, starting with nanomaterials characterisation protocols developed or optimised within the ACEnano project. The platform is publicly available to the scientific community. Other projects are therefore encouraged to use the same concept implemented and optimised in ACEnano.

As described in Deliverable 4.2, the experimental datasets of nanomaterial characterisation are stored together with relevant metadata pertaining to sample preparation, measurement, and the data treatment. The resulting measured value and its metadata will give as complete information as possible so that future reusability of the measured value is maximised. Different types of protocols can be added separately in a questionnaire-like format that guides the user through the documentation process from the preparation and measurement of the sample to data processing:

- Sample preparation: outline of steps that were taken to prepare the original sample for measurement.
- Physicochemical properties measurement protocol: the prepared sample is measured by a technique to yield a value for an endpoint. The measurement is described by technique specific parameters that are crucial for the reproducibility and accuracy of

[4] https://emmc.info/emmo-info/
[5] https://acenano.douglasconnect.com/

endpoint values.

- Data treatment: Description of steps taken to extract the measurement results from raw data.

The protocols submitted to the Knowledge Infrastructure are used to create a complete data workflow by adding the sample identification and description and the experimental results (**Figure 2**). The data warehouse generated is offering long-term storage of data produced by the ACEnano project or provided by the nanosafety community. The data warehouse supports the data harmonisation and the implementation of FAIR principles (Findable, Accessible, Interoperable, and Reusable) towards the goal of generating a reference resource for nanomaterials risk assessment.

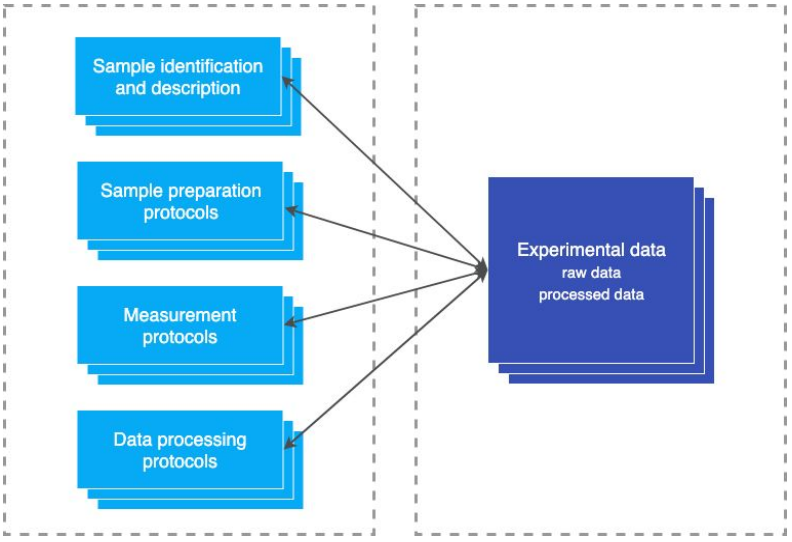

Figure 2. Representation of the ACEnano Knowledge Infrastructure concept

Additional information on the ACEnano Knowledge Infrastructure are available on the platform webpage: https://acenano.douglasconnect.com/about/

To integrate this unique protocols and data warehouse approach within the framework of the NSC and especially make it interoperable with the semantic model of the NanoCommons knowledge infrastructure and other data sources therein, annotation of the protocol description and the (meta)data model is the most important use case of the physicochemical part of the NM ontology. The protocol interface and existing protocols uploaded to the repository were screened for specific terms or groups of terms, which should be stored in a semantically annotated form as part of the protocols and metadata of datasets.

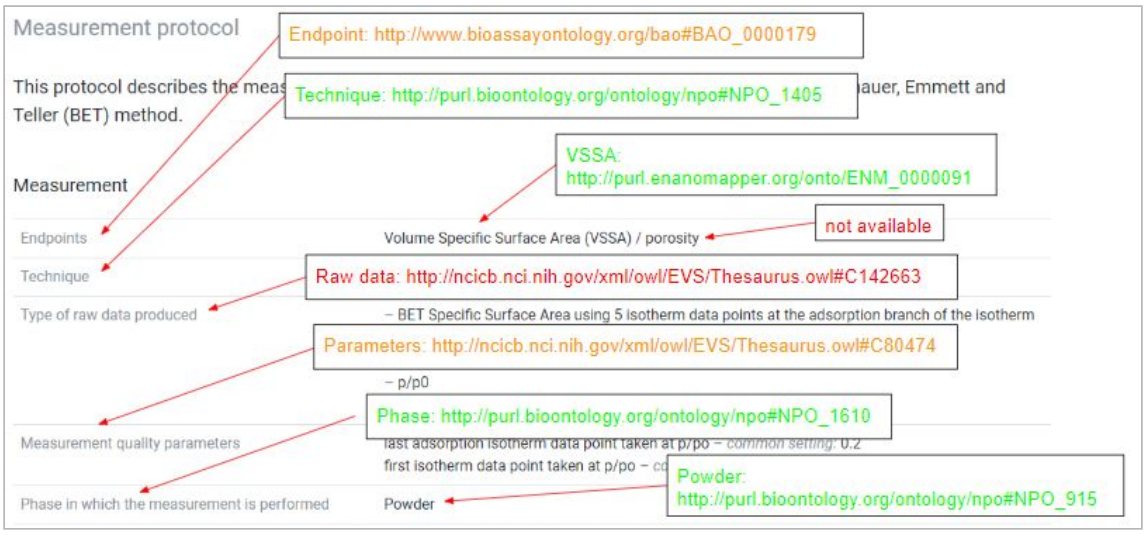

Figure 3. Examples of terminology in the protocol interface to be annotated by the physicochemical characterisation part of NM ontology
(*Green: terms available in existing ontologies; Yellow: terms which should be more refined for their application in the nanosafety area; Red: terms which need to be fully defined by ACEnano*)

2. Use of ontologies in ACEnano

The physicochemical characterisation methods for nanomaterials developed, optimised and standardised in ACEnano have been specifically selected to be used in nanomaterial risk assessment. Therefore, the produced data always has to be linked in a harmonised and interoperable way to other data resources providing hazard, exposure and fate data as e.g., made available in the NanoCommons infrastructure project[6]. These links have also to be manifested in the ontologies used since they provide the semantic model to allow searching across different sources and allow combining and enriching data. Therefore, the goal of the ACEnano ontology activities was not to create a new ontology but to strengthen the physicochemical characterisation area in existing ontologies and, in this way, provide the controlled terminology required for the data annotation and analysis pipelines generated and produced in the other ACEnano work packages and later across the complete nanosafety community, which is completely aligned with ontology activities for hazard, exposure, risk and fate data annotation facilitating data sharing and merging between these areas.

Requirements for the ontology development are at the moment mainly defined by metadata fields in the protocol questionnaires for annotating the chemistries, techniques and related actions, endpoints and units. In the following subsections, the general concept integrates the ACEnano needs into the existing nanosafety ontology landscape. The procedure to identify and collect required terms are presented first in **Section 2.1 and 2.2**. Then, **Section 2.3** contains the workflow used to annotate the questionnaire structure in the ACEnano warehouse. This will allow deep integration into the NanoCommons infrastructure and similar cross-data-warehouse searching and retrieval tools based on semantic interoperability concepts. **Section 2.4** described strategies and workflows on how to handle and complete

[6] https://www.nanocommons.eu/

terms required for the warehouse annotation but also for the physicochemical characterisation of nanomaterials in general, which are not integrated in existing ontologies up to now or have incomplete entries (e.g. missing definitions). Finally, a tool to support the annotation of protocols and data during their upload onto the ACEnano warehouse is described in **Section 2.5**.

2.1 Ontology development concepts

At the time of this writing, eNanoMapper is, to our knowledge, the most comprehensive ontology[7] in the area of nanosafety and perhaps even in chemical and nanomaterial risk assessment and has been endorsed by many members of the nanosafety community as the starting point for further developments and extensions. Therefore, the ACEnano activities are also building on top of this ontology and the concepts and processes adopted therein. The technical framework from the eNanoMapper project provides full functionality for development, versioning and dissemination of the ontology as well as the reuse of existing ontologies to avoid unnecessary and divisive re-implementation. To continue the work, maintaining and sustaining the ontology after the end of the eNanoMapper project, the infrastructure project NanoCommons took over responsibility for the eNanoMapper ontology in January 2018 and ACEnano is intensively collaborating with NanoCommons to provide the ACEnano additions and updates to the users as soon as possible in an iterative and ongoing process.

Such close interactions between the domain experts from ACEnano and the ontology experts from NanoCommons is of uttermost importance to integrate the physicochemical characterisation part smoothly with the existing parts and other new entries coming from the other NanoSafety projects based on the quality-control rules implemented in the eNanoMapper development workflows and enforced by the NanoCommons team. Such strict rules are needed mainly because of two concepts forming the pillars of eNanoMapper: 1) the taxonomy concept adopted by all major ontologies and 2) the reuse of parts of existing ontologies and definition of new terms only if nothing appropriate exists.

[7] eNanoMapper ontology (Version 6.0; last update: 30-Aug-2019)
http://bioportal.bioontology.org/ontologies/ENM/

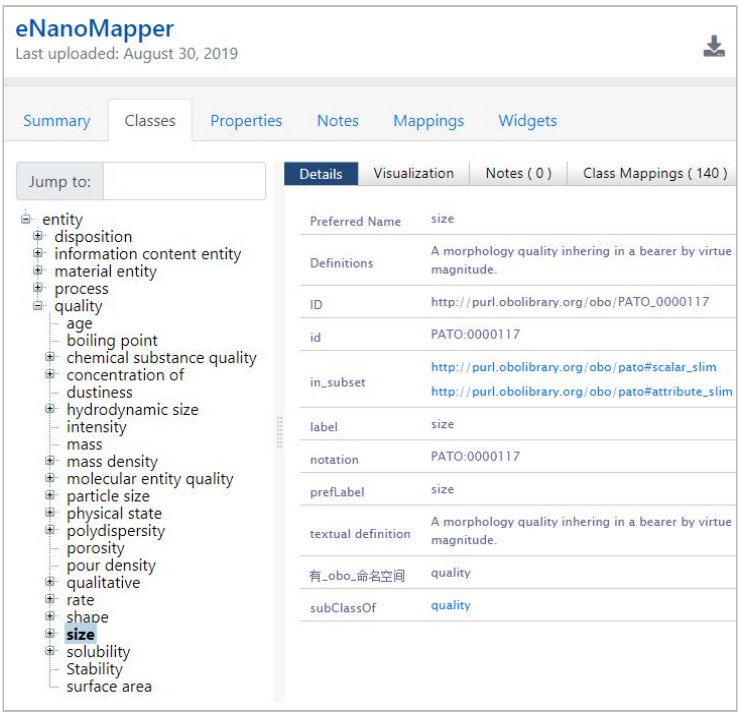

Figure 4. Subset of the taxonomy used in the eNanoMapper ontology

A taxonomy is a classification of things in a hierarchical form. It is usually a tree or a lattice that expresses subsumption relation - i.e., A subsumes B meaning that everything that is in A is also in B. An example is shown in **Figure 4**. Size is a subsumption of quality, which is itself a subsumption of entity being the most upper concept of the eNanoMapper ontology. This suggests that all properties of "quantity" are inherited by "size", which can then define additional properties. For the consistency of the ontology, new terms have to be correctly fitted into this taxonomy since the meaning of the term is not only determined by the description of the term but also its location and relationship to the higher concepts. Thus, the position in the taxonomy tree also determines if a specific term can be reused from another ontology since the higher-level concepts can give a more generic term a more specific meaning. For example, the term "endpoint" is grouped under the higher-level concepts "terminal point", "point" and finally "geometric object" in the Semanticscience Integrated Ontology[8]. "Endpoint" has therefore, a clearly different meaning as in the BioAssay Ontology[9], where it is grouped under assay result component corresponding to the usage of the term in the NanoSafety community. However, for ACEnano, an even more specific term to limit it to physicochemical characterisation endpoints is beneficial (see **Section 2.4** below on complex ontology terms).

eNanoMapper is an application ontology. It was built with the goal of fulfilling the specific application use case of annotation of a database and software tool used in the nanosafety area and specifically the eNanoMapper tools. However, with the extensions performed in ongoing projects including ACEnano, it could be extended to become a domain ontology beneficial for all applications of ontologies in the nanosafety area. Both application and domain ontologies

[8] https://bioportal.bioontology.org/ontologies/SIO
[9] https://bioportal.bioontology.org/ontologies/BAO

often combine chunks of several reference ontologies including upper or top-level ontology, which consists of very general terms. The hierarchy of ontologies is depicted in **Figure 5**. At the time of this writing, eNanoMapper includes 27 third-party ontologies including Ontology of Adverse Events (OAE, 4166 reused classes), Experimental Factor Ontology (EFO, 2652 reused classes), Ontology for Biomedical Investigations (OBI, 803 reused classes) and Environment Ontology (ENVO, 647 reused classes). This overlap shows the concentration of the existing eNanoMapper ontology on adversity (hazard), investigations using bioassays and environmental aspects recently integrated through collaborations with projects like NanoFase and NanoInformatics Knowledge Commons (NIKC). Physicochemical characterisation as coming in now from ACEnano should continue to strongly apply the reusing concept but has to take care that higher-level ontologies additionally added to cover these aspects or at least the relevant parts of them can be integrated without inconsistencies in the hierarchy defined by the eNanoMapper taxonomy.

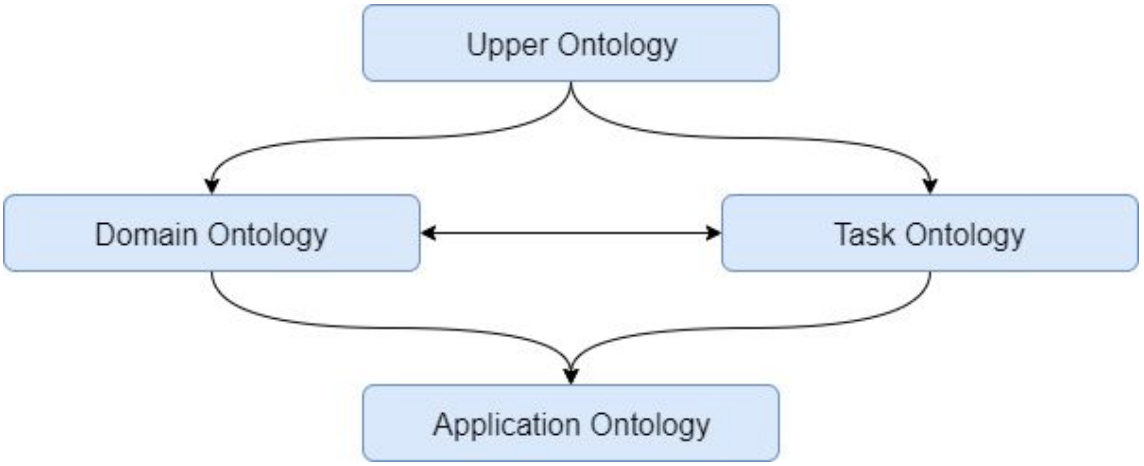

Figure 5. Hierarchy of ontologies:
terms from the most general upper ontologies, applicable in many domains, are re-used by domain and task ontologies, domain and task ontologies exchange terminology and application ontologies used for a very specific purpose are re-using terms from domain and task ontologies and therefore, indirectly from upper ontologies

2.2 Identification of required terms and community-curated descriptions

The focus for a first round of physicochemical ontology development and improvement was put on the terms that are essential for the identification of relevant protocols (experimental method, nanomaterial pre-characterisation to select appropriate methods, etc.) and to compare different variants of the protocols on a high level (e.g., effect of different sample preparation steps influencing the results, etc.). Manual search for these terms showed that annotation of starting materials is possible to a large extent with terms available in the eNanoMapper ontology, while experimental setups and parameters needed to include terms from other ontologies are not covered at all at the moment. For these not yet included or missing terms, the specific expertise of all partners was exploited to evaluate if a term and the corresponding definition to be transferred and included into eNanoMapper are exactly corresponding to the understanding of the term by the expert and are specific enough, clear and unambiguous. Problematic cases were discussed by multiple experts until consensus of the prefered human-readable term to use and wording of the definition was reached. The generated list of required new ontology terms (see **Annex 1**) was evaluated by NanoCommons ontology experts and prepared for integration into the next NanoCommons release of the eNanoMapper ontology. Additionally, since some of the terms in existing ontologies are lacking, which allows different interpretation and hinders their unambiguous usage, the list also includes terms with added and improved (with respect to their clarity) definitions, which will now be fed back into the original ontologies, either eNanoMapper or ontologies integrated therein, to prevent incorrect usage leading to incorrect linkage between data.

Developing a new ontology or, as done here, integrating an underdeveloped area in an existing ontology needs to start with outlining the hierarchical structure of the taxonomy to be used and, in the latter case, aligning it with the existing layers of concepts and classes. This can only be done after a representative corpus of terminology has been collected as done in the first round of development resulting in the list in **Annex 1** separate to the standard streams for continuous extension and improvement of the eNanoMapper ontology. Now that this was successfully achieved and the eNanoMapper taxonomy has been proven to be flexible enough to accommodate physico-chemical characterisation terminology, we will switch back to a more formal ontology development in ACEnano, where all users from ACEnano but also from third-parties using the publicly accessible version of the data warehouse will be able to use an issue tracker for the submission of requests for adding, merging and updating ontology entries and the mailing list to discuss ontology content with interested community participants and third parties. This manual curation will now also be supported by text mining technologies to extract additional information from published sources to disambiguate and map semantic concepts, acronym resolutions and term permutations and to facilitate the harmonisation with the ongoing work in the nanosafety and general toxicology field. Even if semi-automatisation can be obtained with text mining tools, there is still the need for a significant manual curation effort that is aided by crowd-sourcing activities across the NanoSafety Cluster and advertised and disseminated through the training sessions and hackathons organised by NanoCommons and OpenRiskNet with the support by ACEnano (see **Section 3** below).

2.3 ACEnano protocols and data warehouse annotation process

State-of-the-art concepts were developed for data sharing following the FAIR principles. Special emphisis was put on providing interfaces used by services searching and accessing data across different data warehouses as developed e.g. in the Nanocommons project. Such meta-searches have the highly increased complexity that these underlying data warehouses are based on different technology and are developed and provided by different organisations and projects. This is achieved by basing the warehouse on semantic models to link relevant information e.g., for a specific material in all these warehouses instead of trying to fit all the data into the same data warehouse. The data but even more importantly the database model and the metadata related to the data has to be annotated to understand where and how the information is stored, how to build the inter-database links, find the corresponding data and provide the enriched, combined datasets. In ACEnano, this annotation is done on multiple layers. The highest level is the annotation of the protocol questionnaires, which is presented here while the data annotation is described in **Section 2.5**. **Figure 3** already showed needed annotations for the protocols. On the one hand, the questionnaire structure has to be annotated so that meta-services such as the NanoCommons knowledge infrastructure can understand which field has to be queried to get specific details such as the physicochemical endpoint measured or the technique applied. On the other hand, also the specific entries selected in a protocol should be annotated, e.g. “volume specific surface area” measured with this protocol, to be able to combine and compare similar experiments stored within the same or different data warehouses. **Figure 6 and 7** give additional examples for sample identification annotation, respectively.

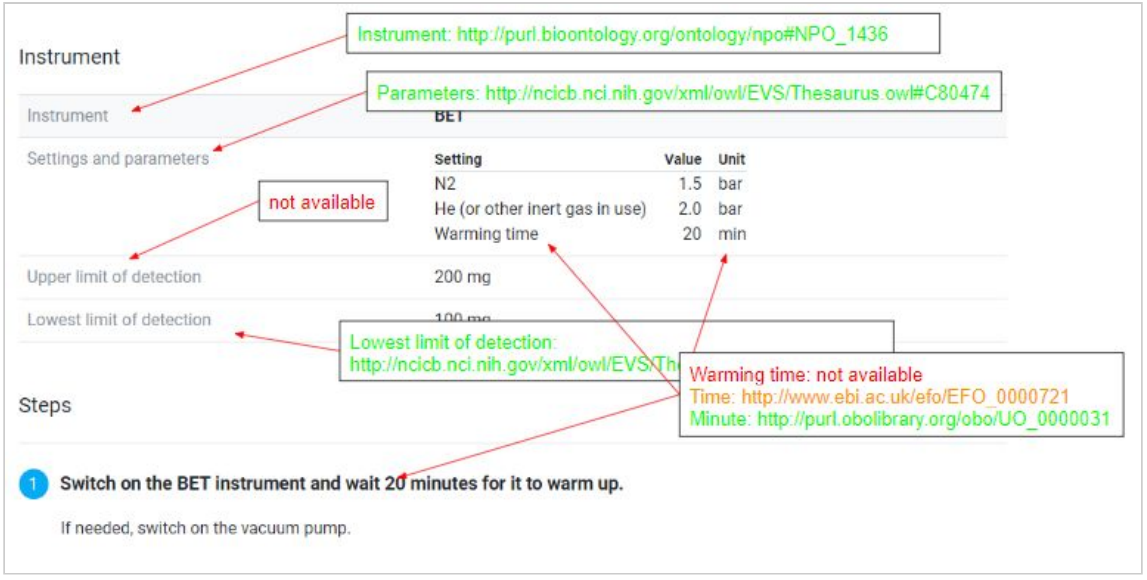

Figure 6. Examples for annotations needed in the instrument section of ACEnano protocol questionnaires

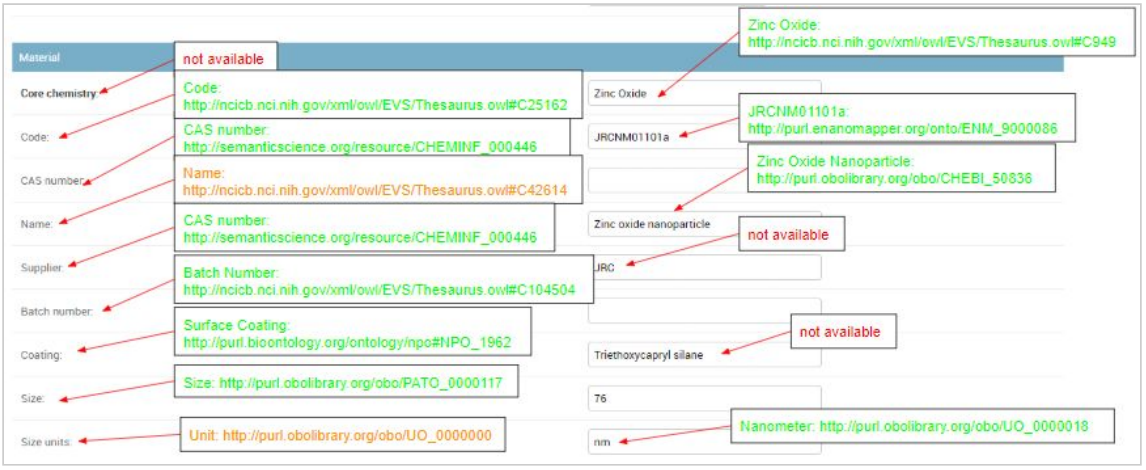

Figure 7. Examples for annotations needed in the sample identification section of ACEnano protocol questionnaires

The questionnaire structure is defined for a specific technique - endpoint combination within the ACEnano data warehouse. Moreover, possible selections for specific fields are often provided as drop-down lists. The annotation of the structure and these predefined fields is thus a one-time effort performed during the data warehouse development during which new experimental methods are specified and integrated (Annotation of user-provided metadata and data is supported by the Ontology Lookup Service described in **Section 2.5**). Each field to be annotated is represented in the setup of the protocol module of the ACEnano protocols and data warehouse as a pair of field name and Uniform Resource Identifier (URI) as used in the ontology as the identifier for the term. Two examples are given in **Figure 8**.

A

B

Figure 8. Annotation of protocol questionnaires in the protocol module of the ACEnano protocols and data warehouse.
The first example (A) shows the annotation of the physicochemical characterisation endpoint name "Particle Size Distribution" while the second (B) gives the annotation for "Viscosity" also including the annotation for the corresponding unit.

Missing or less specific ontology terms can be added and updated at any time by the administrators of the warehouse to represent the new ontology developments discussed above.

The annotation performed for the questionnaire structure and predefined terms included the following steps:

1. Pick and record terms that are essential for nanomaterial analysis and characterisation by screening the protocol interface and the uploaded protocols;
2. Manually search in the BioPortal[10] comprehensive repository of biomedical ontologies (**Figure 9**);

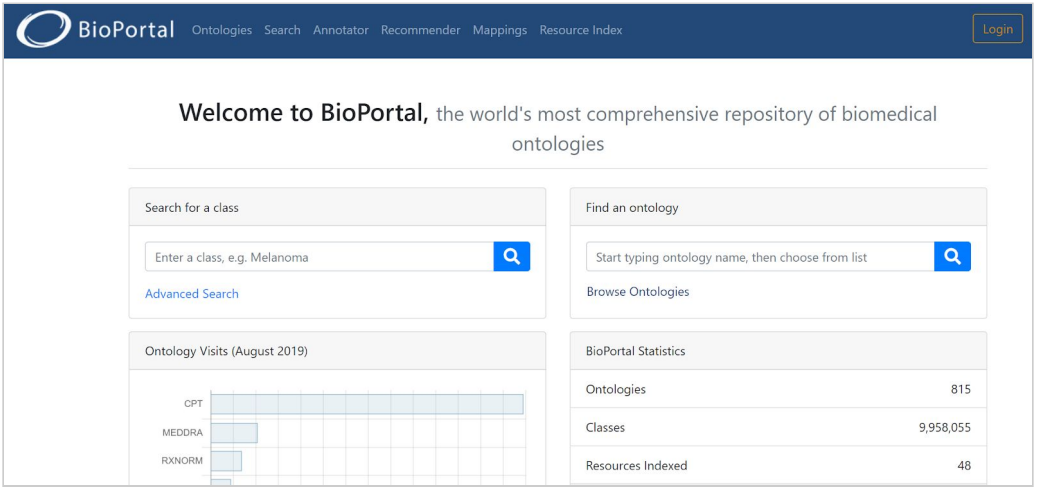

Figure 9. Search page in the BioPortal ontology repository

3. Prioritisation of terms found in the eNanoMapper ontology directly guaranteeing alignment and harmonisation with the other NanoSafety Cluster projects and especially NanoCommons. Annotation of starting materials was possible to a large extent from eNanoMapper (**Figure 10**);

[10] https://bioportal.bioontology.org/

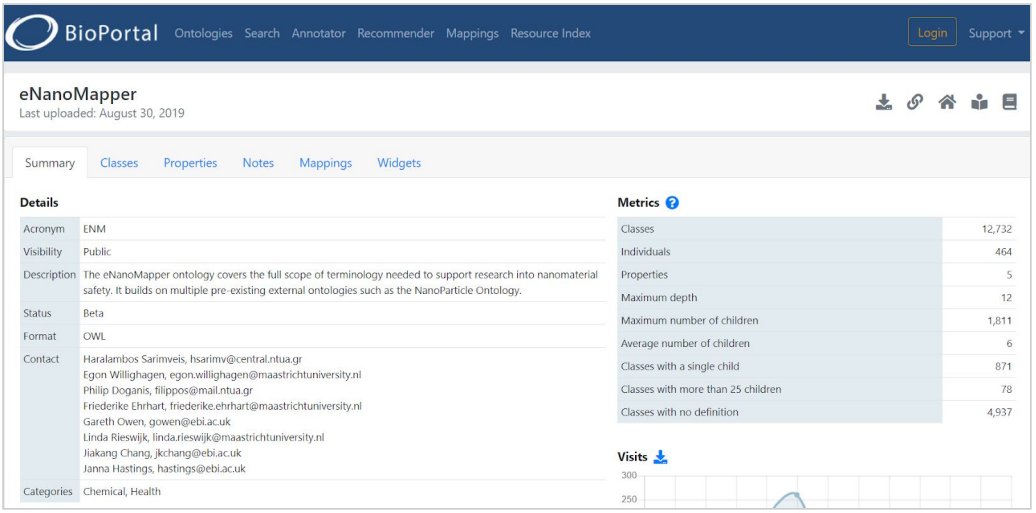

Figure 10. Starting page of eNanoMapper ontology in BioPortal

4. Treat separately terms which lack definitions or are not available in eNanoMapper (see **Section 2.4** below);
5. For the terms being present and complete in eNanoMapper, record details (e.g., in a separate file to facilitate the process) including the terms name, URI as ID and definition (**Figure 11**);

Terms found in eNanoMapper	eNanoMapper ID URL	eNanoMapper Description
Endpoints	http://www.bioassayontology.org/bao#BAO_0000179	The endpoint is a quantitive or qualitative interpretable standardized representation of a perturbation (a change fro defined reference state of a "closed" model system) that is measured by the bioassay. An endpoint consists of a s data points, one for each perturbing agent (screened entity) tested the assay.
Frequency	http://purl.obolibrary.org/obo/PATO_0000044	A physical quality which inheres in a bearer by virtue of the number of the bearer's repetitive actions in a particular
Incubation	http://purl.bioontology.org/ontology/npo#NPO_2000	A technique used for incubating mixtures in an assay.
Inductively Coupled Plasma Mass Spectrometry	http://purl.obolibrary.org/obo/CHMO_0000538	Plasma mass spectrometry where the plasma has been generated by electromagnetic induction.
Laser Ablation Inductively Coupled Plasma Mass Spectrometry	http://purl.obolibrary.org/obo/CHMO_0000550	Mass spectrometry where the sample is vaporised using a laser pulse then ionised in a plasma (a partially ionised gas---such as Ar---containing free electrons) which has been generated by electromagnetic induction.
ROS generation	http://purl.obolibrary.org/obo/CHEBI_70982	Any entity used to generate reactive oxygen species.
Solubility/dissolution	http://purl.obolibrary.org/obo/PATO_0001536, http://purl.bioontology.org/ontology/npo#NPO_1955	"A molecular quality that inheres in a molecular entity by virtue of the bearer's disposition to dissolve in a liquid." N
Solvent	http://purl.obolibrary.org/obo/CHEBI_46787	A liquid that can dissolve other substances (solutes) without any change in their chemical composition.
Technique	http://purl.bioontology.org/ontology/npo#NPO_1405	A systematic procedure or a practical method which is used for accomplishing a task.
Transmission Electron Microscopy	http://purl.bioontology.org/ontology/npo#NPO_1430	A light source at the top of the TEM emits the electrons that travel through vacuum in the column of the microscop Instead of glass lenses focusing the light in the light microscope, the TEM uses electromagnetic lenses to focus th electrons into a very thin beam. The electron beam then travels through the specimen you want to study. Dependir the density of the material present, some of the electrons are scattered and disappear from the beam. At the botto microscope the unscattered electrons hit a fluorescent screen, which gives rise to a shadow image of the specime different parts displayed in varied darkness according to their density. The image can be studied directly by the op photographed with a camera.
Ultraviolet–visible spectroscopy	http://purl.org/obo/owl/FIX#FIX_0000016	An absorption spectroscopic technique in which the irradiating light has wavelengths within the ultraviolet and visib regions of the electromagnetic spectrum

Figure 11. Collection of information on the existing terms to be annotated

6. Perform annotation by storing the ID (and definition, if the form allows) of the term in the ontology fields of the protocols module of the ACEnano protocols and data warehouse accessible via the admin interface (**Figure 12**). Currently, the ontology annotation is possible for Action parameters, Actions, Analysis, Chemistries, Measurement equipment, Measurement protocols, Media, Phases, Protocol endpoints, Protocol techniques, Sample Preparation Protocol actions, Samples models and for the corresponding units.

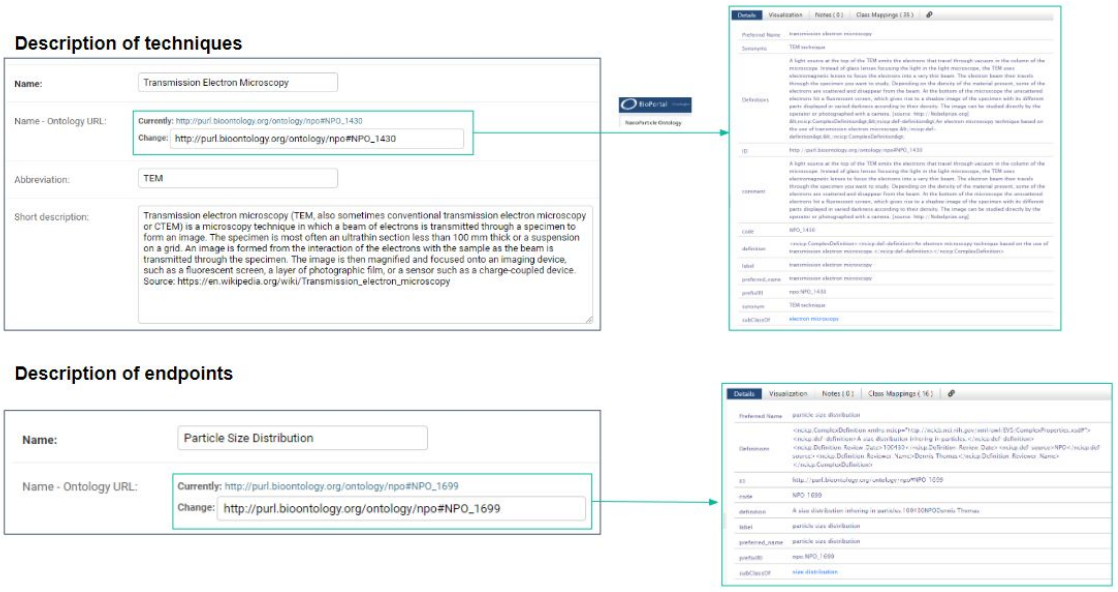

Figure 12. Annotation performed in the admin interface of ACEnano Knowledge Infrastructure

2.4 Improvement of the eNanoMapper ontology to cover physicochemical characterisation

As described above, many ontology terms were already available in the eNanoMapper ontology especially for defining the starting material and others can be found in ontologies, which are already partly integrated in eNanoMapper, or other, which could be added to the list of ontologies from which terms are reused. However, for all these terms, their appropriateness for the application in ACEnano has to be evaluated before using them in protocol and data annotation. Additionally, missing terms combined with unambiguous descriptions have to be added to make the ontology more complete also for the physicochemical characterisation area. Experts on specific methods and nanomaterial characterisation, in general from the ACEnano project, were consulted and asked to review the existing ontology entries or provide preferred terms and corresponding descriptions. To support the work of the experts, a screening of terms required for annotation of the ACEnano warehouse across all ontologies available on BioPortal was performed by the ontology team of WP4 and collected in a spreadsheet for the experts to evaluate, correct, clarify and comment on.

The following steps were performed in order to create the first version of the spreadsheet provided by the ontology team:

1. Provide the ontology term and description from eNanoMapper matching the required term in the warehouse;
2. For terms on which the annotation was not found in eNanoMapper but in other ontologies, consider ontologies (partly) integrated into eNanoMapper with priority. Integrating terms from such ontologies (e.g. Chemical Methods Ontology (CHMO), NanoParticle Ontology (NPO), National Cancer Institute Thesaurus (NCIT)) ease the addition process of the new terms based on already proven interoperability between

these ontologies and eNanoMapper (see eNanoMapper tutorial[11] for more information);

3. For terms that annotations could not be found in ontologies contained in eNanoMapper, consider the ontology which provide the best definition for the searched term;
4. For terms that no proper annotation could be found at all in BioPortal (e.g., mostly in the case of composed terms or group of words which describe a single concept such as experimental techniques and parameters), initiate the enhancement of the eNanoMapper ontology. This was done, for example, by generating ontology terms for composed terms such as Brunauer–Emmett–Teller analysis or CO_2 concentration. These terms were developed in collaboration with the OpenRiskNet and NanoCommons projects. Specific Uniform Resource Identifiers (URI) were thus generated for the complete term but this approach also keeps information including URI if available on the individual components such as “analysis” and “concentration”, which can be used in reasoning and grouping of different analyses and concentrations. More information can be found on the OpenRiskNet wiki pages[12]).

The expert review resulted in different needs for integration of specific terms:

1. When the terms are available in eNanoMapper
    a. A clear description corresponding to the usage in ACEnano exists: No additional action is needed and the term can directly be used in the ACEnano warehouse;
    b. The term is available but the description is missing, misleading or describing another use of the term: New, updated descriptions are provided by the experts. In the latter case, it is checked if the original use is needed in eNanoMapper requiring two separate terms or can be replaced.
2. When the terms are available in other ontologies already integrated or not in eNanoMapper:
    a. Description corresponds to the usage in ACEnano: Terms are marked as possible additions and discussed with the NanoCommons project;
    b. Description not existing or misleading/describing another usage of the term: These cases are handled in the same way as non-existing terms.
3. When the terms are not available in any existing ontology: experts are providing preferred term and clear descriptions, which are first discussed with additional experts within ACEnano and then opened for comments by the community.

Terms from the first annotation round falling into group 1b, 2 and 3 have now been proposed for inclusion or updating/improvement in the eNanoMapper ontology using the normal workflow for proposing, reviewing, including and quality-checking guided and supervised by NanoCommons. Group 2a (20 new terms) was successfully integrated in the development version of eNanoMapper and will become part of the official ontology with the next release. Around 70 other terms from group 2b and 3 are on the waiting list for integration including composed terms. Participants of the NSC ontology hackathon on 13 December 2019 (see below) have had additional discussions on their descriptions, deciding if similar terms should

[11] https://tess.elixir-europe.org/materials/adding-ontology-terms
[12] https://github.com/OpenRiskNet/home/wiki/Modelling-IC50-results

be added at the same time and select the specific location in the taxonomy, where the terms should be added. For terms, which are re-used from ontologies other than eNanoMapper, it is planned to provide the improved descriptions to the original developers of these ontologies so that the improvements can be made on this level and will be available in eNanoMapper, when the updated parent ontology is re-integrated.

2.5 Use of Ontology Lookup Service

Annotation described so far was done for terms building a central part of the warehouse infrastructure, the questionnaires or coming from predefined list. However, additional information and metadata on specific datasets is provided by the user at the time of protocols and data upload. Therefore, the terms used are not limited to a predefined list and the corresponding ontology term/URI lists cannot be generated as a one-time activity. Instead, guiding the user to prioritise terms as they are defined in ontologies over other synonyms and support requesting of non-existing terms has to be done on-the-fly. For doing so, the ACEnano warehouse has integrated the EMBL-EBI Ontology Lookup Service (OLS)[13] at all the places where a term from a controlled dictionary is expected.

OLS gives access to a repository for ontologies, mainly biomedical but also e.g. the eNanoMapper ontology, with the aim to provide a single point of access to the latest ontology versions. It is an open source interoperable service that can be browsed through the website or used programmatically via the OLS API.

OLS is integrated in the ACEnano KI and uses a term search engine making the automated annotation possible. It performs a search and auto completes the entry when the users start to type a few letters in several boxes of the protocols (e.g. “Units”) and data (e.g. nanomaterial “Name”, etc) questionnaires. The user can choose the preferred term from the generated drop-down list as shown in **Figure 13**.

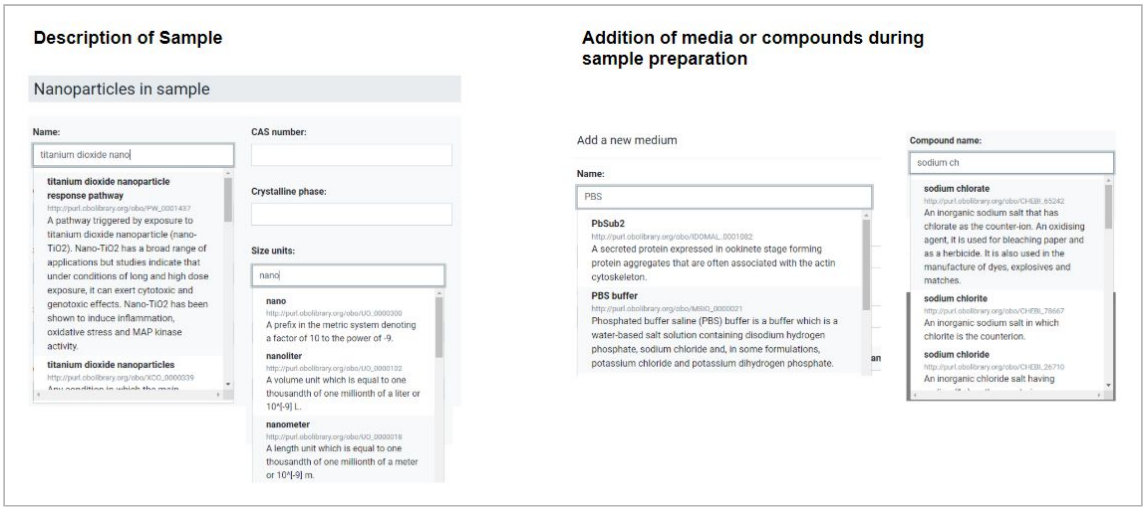

Figure 13. Examples of the use of the EMBL-EBI Ontology Lookup Service inside the ACEnano protocols and data warehouse

[13] https://www.ebi.ac.uk/ols/index

3. Ontology training sessions

ACEnano partners involved in the ontology task are following closely and support the training activities or hackathons in this area, as part of the collaborative work established within the NSC framework. A few examples of such activities focused on ontologies, where ACEnano project partners were involved actively, are included in **Table 1**. The resources and knowledge gained in these sessions were further used for the developments in ACEnano. Additionally, ontology aspects were included in the ACEnano data warehouse training first given internally at the general assembly in Gijon and then publicly at the NanoSafety Cluster week in Copenhagen. The advantages of being actively involved in these training activities are that partners from the other ACEnano work packages could be easier motivated to participate, the training materials could be re-used in internal and public ACEnano trainings and concepts important for the annotation of the ACEnano warehouse such as complex, composed terms were prioritised in the discussions.

Table 1. Relevant events on the ontology areas joined by ACEnano partners

Event	Date and location	Short description
1st NanoCommons Hackathon on "Ontological Annotation of Datasets" https://www.nanocommons.eu/1st-nanocommons-hackathon-ontological-annotations-of-datasets/	9 Oct 2018 (Athens, Greece)	This event was co-organised by NanoCommons and OpenRiskNet projects. The participants worked using their own or mock datasets and search through established ontologies (e.g. eNanoMapper Ontology) for ontological annotations. The participants also learn how to prepare electronic files (e.g. JSON) containing the raw data and the ontological metadata.
OpenRiskNet/NanoCommons ontology meeting https://openrisknet.org/events/45/	13-14 Dec 2018 (Brussels, Belgium)	The goal of this meeting was to get a picture of the ongoing ontology activities in the toxicology area, harmonize these efforts and the developed ontologies therein and extend the existing toxicology ontology with missing terms, write up guidance documents, and annotate data sets. The following specific topics were covered: 1. What ontologies are out there and can we combine them to a toxicology application ontology; 2. Data and software schema: How much ontology do we need to annotate complex services; 3. Ontology Hacking.
Data Management Training (organised prior to the annual meeting of ACEnano consortium)	25 September 2019 (Gijon, Spain)	The event was addressed to ACEnano project members only. The aim was to introduce the Knowledge Infrastructure to the project members that are involved in the experimental work and support them in adding protocols, creating data workflows and uploading data. The

		second aim is to understand more on the protocols and data annotations and the use of ontologies in the context of ACEnano.
ACEnano Protocols and Data Warehouse Training (during the "NanoSafety Week") https://infrastructure.nanocommons.eu/events/7/nanosafety-cluster-week/	10 Oct 2019 (Copenhagen, Denmark)	The aim was to introduce unique approach of the ACEnano Knowledge Protocols and Data warehouse designed to disseminate protocols and their variations and to store, manage and share data for physicochemical characterisation of nanomaterials under standard conditions as well as at different life stages.
NSC ontology hackathon	13 Dec 2019 (Online, via GoToMeeting)	This virtual hackathon organised by Maastricht University in the context of NSC working Group F aims to clarify several aspects of the addition of missing or new terms to the eNanoMapper ontology (i.e., terms suggested by participants). A webinar "Using axioms for computational descriptors" is also included. A set of tutorials were provided to participants: ● https://github.com/NanoCommons/tutorials ● https://enanomapper.github.io/tutorials/

Conclusions

Assessing nanomaterial safety is a challenge only addressable by a multidisciplinary community. It needs to evaluate data for physicochemical characterisation, hazard, exposure and fate. An effective combination of this data coming from multiple sources is only possible based on a common use of terminology and common understanding of the concepts behind these terms formalised in a nanosafety ontology. There exist many ongoing activities to develop such an ontology and this effort started within the eNanoMapper project and is now continued by other projects of the EU NanoSafety Cluster coordinated by NanoCommons. Due to the strong focus of ACEnano on methodology and specifically physicochemical characterisation, ACEnano took the lead in developing the relevant part of the ontology in close collaboration and aligned with other nanosafety ontology activities, mainly driven by the need to provide semantic annotations of the protocols, metadata and data stored in the ACEnano data warehouse. This approach makes the ACEnano warehouse interoperable with other data sources as provided e.g. as part of the NanoCommons knowledge platform. Clear workflows on how to prioritise existing terms from different ontologies for such annotation or to generate new, more specific ones and integrate them into the eNanoMapper ontology have been defined. Resulting new terms and (updated) definitions specifically for ACEnano methodology have been provided to the NanoCommons team managing the eNanoMapper ontology and are currently being added. Additionally, guidelines for annotation of protocols and data uploaded to the ACEnano warehouse have been provided to all partners and ontology lookup services have been integrated into the user interface to facilitate the annotation process and guiding the user to the preferred terminology if multiple ontology terms or terms with different specificity exist. Finally, this has been complemented by different workshops and hackathons partly organised in collaboration with other projects to train the experimental partners in the use of ontologies and the annotation process.

References

1. Contributors to Wikimedia projects. Ontology (information science) - Wikipedia. In: Wikimedia Foundation, Inc. [Internet]. 19 Apr 2002. Available: https://en.wikipedia.org/wiki/Ontology_(information_science)

2. Hastings J, Jeliazkova N, Owen G, Tsiliki G, Munteanu CR, Steinbeck C, et al. eNanoMapper: harnessing ontologies to enable data integration for nanomaterial risk assessment. J Biomed Semantics. 2015;6: 10.

Annexes

Annex 1. ACEnano ontology terms

Protocols Terms	Annotated in the admin interface	Ontology URL		BioPortal Description	Comparation Descriptions	Specialists Description
Ion-selective electrode		http://purl.obolibrary.org/obo/CHMO_0002393	CHMO	An electrode which responds to the activity of a primary ion in presence of various other (interfering) ions in the sample solution. Ion-selective electrodes contain a selective membrane which contains fixed or mobile sites that interact with ions in solution.	Missing Specialist	NA
Technique		http://purl.bioontology.org/ontology/npo#NPO_1405	ENM	A systematic procedure or a practical method which is used for accomplishing a task.	OK	An approach to perform a method
Frequency	Yes	http://purl.obolibrary.org/obo/PATO_0000044	ENM	A physical quality which inheres in a bearer by virtue of the number of the bearer's repetitive actions in a particular time.	OK	The number of repeating occurances of an event per time unit
ROS generation	Yes	http://purl.obolibrary.org/obo/CHEBI_70982	ENM	Any entity used to generate reactive oxygen species.	OK	Any entity used to generate reactive oxygen species.
Solubility/dissolution	**Only Solubility; it seems I cannot add 2 URLs; also for dissolution will give error**	http://purl.obolibrary.org/obo/PATO_0001536, http://purl.bioontology.org/ontology/npo#NPO_1955	ENM	"A molecular quality that inheres in a molecular entity by virtue of the bearer's disposition to dissolve in a liquid." NA	OK	"A molecular quality that inheres in a molecular entity by virtue of the bearer's disposition to dissolve in a liquid." NA
Inductively Coupled Plasma Mass Spectrometry	Yes	http://purl.obolibrary.org/obo/CHMO_0000538	ENM	Plasma mass spectrometry where the plasma has been generated by electromagnetic induction.	OK	Plasma mass spectrometry where the plasma has been generated by electromagnetic induction.
Laser Ablation Inductively Coupled Plasma Mass Spectrometry	Yes	http://purl.obolibrary.org/obo/CHMO_0000550	ENM	Mass spectrometry where the sample is vaporised using a laser pulse then ionised in a plasma (a partially ionised gas---such as Ar---containing free electrons) which has been generated by electromagnetic induction.	OK	Mass spectrometry where the sample is vaporised using a laser pulse then ionised in a plasma (a partially ionised gas---such as Ar---containing free electrons) which has been generated by electromagnetic induction.
Transmission Electron Microscopy	Yes	http://purl.bioontology.org/ontology/npo#NPO_1430	ENM	A light source at the top of the TEM emits the electrons that travel through vacuum in the column of the microscope. Instead of glass lenses focusing the light in the light microscope, the TEM uses electromagnetic lenses to focus the electrons into a very thin beam. The electron beam then travels through the specimen you want to study. Depending on the density of the material present, some of the electrons are scattered and disappear from the beam. At the bottom of the microscope the unscattered electrons hit a fluorescent screen, which gives rise to a shadow image of the specimen with its different parts displayed in varied darkness according to their density. The image can be studied directly by the operator or photographed with a camera.	OK	A light source at the top of the TEM emits the electrons that travel through vacuum in the column of the microscope. Instead of glass lenses focusing the light in the light microscope, the TEM uses electromagnetic lenses to focus the electrons into a very thin beam. The electron beam then travels through the specimen you want to study. Depending on the density of the material present, some of the electrons are scattered and disappear from the beam. At the bottom of the microscope the unscattered electrons hit a fluorescent screen, which gives rise to a shadow image of the specimen with its different parts displayed in varied darkness according to their density. The image can be studied directly by the operator or photographed with a camera.
Solvent		http://purl.obolibrary.org/obo/CHEBI_46787	ENM	A liquid that can dissolve other substances (solutes) without any change in their chemical composition.	OK	A liquid (typically) in which a solute will dissolve to form a solution
Density	Yes	http://purl.enanomapper.org/onto/ENM_0000084	ENM	NA	Missing in BioPortal	Mass per unit of volume
Drying	Yes	http://purl.bioontology.org/ontology/npo#NPO_1956	ENM	NA	Missing in BioPortal	The removal of water or solvent from a sample by evaporation
Vortexing	Yes	http://purl.bioontology.org/ontology/npo#NPO_1952	ENM	NA	Missing in BioPortal	The mixing of liquids to produce a more homogenous sample using cyclic motion to produce a vortex
Sonication	Yes	http://purl.bioontology.org/ontology/npo#NPO_1961	ENM	NA	Missing in BioPortal	The use of sound energy typically ultra hgh frequency to agitate or mix samples
Heating	Yes	http://purl.bioontology.org/ontology/npo#NPO_1958	ENM	NA	Missing in BioPortal	Increasing temperature
Shaking	Yes	http://purl.bioontology.org/ontology/npo#NPO_1951	ENM	NA	Missing in BioPortal	Agitation of a sample
Isoelectric Point	Yes	http://purl.bioontology.org/ontology/npo#NPO_1204	ENM	NA	Missing in BioPortal	pH at which a molecule exhibits no net electrical charge
Capillary electrophoresis	Yes	http://purl.org/obo/owl/FIX#FIX_0000836	ENM	NA	Missing in BioPortal	Separation technique based upon electrophoretic mobility of a analyte across a large potential difference
Dynamic Light Scattering	Yes	http://purl.bioontology.org/ontology/npo#NPO_1469	ENM	NA	Missing in BioPortal	Particle sizing technique based on Brownian motion and scattered light
Batch dispersion / stability	Only Batch dispersion	http://purl.enanomapper.org/onto/ENM_0000081	ENM	NA	Missing Both	NA
Crystalline phase	Yes	http://purl.enanomapper.org/onto/ENM_0000083	ENM	NA	Missing Both	NA
Particle Size Distribution	Yes	http://purl.bioontology.org/ontology/npo#NPO_1699	ENM	NA	Missing Both	NA
Particle (number) concentration	Yes	http://purl.bioontology.org/ontology/npo#NPO_1830	ENM	NA	Missing Both	NA
Z-potential	Yes	http://purl.enanomapper.org/onto/ENM_0000092	ENM	NA	Missing Both	NA
Atomic Force Microscopy	Yes	http://purl.bioontology.org/ontology/npo#NPO_1434	ENM	NA	Missing Both	NA

Protocols Terms	Annotated in the admin interface	Ontology URL		BioPortal Description	Comparation Descriptions	Specialists Description
Raman spectroscopy	Yes	http://purl.org/obo/owl/FIX#FIX_0000058	ENM	NA	Missing Both	NA
Scanning Electron Microscopy	Yes	http://purl.bioontology.org/ontology/npo#NPO_1429	ENM	NA	Missing Both	NA
Endpoints	No	http://www.bioassayontology.org/bao#BAO_0000179	ENM	The endpoint is a quantitive or qualitative interpretable standardized representation of a perturbation (a change from a defined reference state of a "closed" model system) that is measured by the bioassay. An endpoint consists of a series of data points, one for each perturbing agent (screened entity) tested the assay.	A bit different	The conclusion of a chemical reaction or a defined target outcome of an experiment; 2. An endpoint is the final stage of a period or process, i.e. in terms of ecotox testing such as reproduction success, mortality, growth or growth inhibition.
Incubation	Yes	http://purl.bioontology.org/ontology/npo#NPO_2000	ENM	A technique used for incubating mixtures in an assay.	A bit different	The maintinence of environmental conditions such as temperature, humidity and pressure for the development of biological assays
Ultraviolet–visible spectroscopy	Yes	http://purl.org/obo/owl/FIX#FIX_0000016	ENM	An absorption spectroscopic technique in which the irradiating light has wavelengths within the ultraviolet and visible regions of the electromagnetic spectrum	A bit different	Exciting electrons by means of radiation and recording the attenuated light resulting in a plotted graph of absorbance versus wavelength
Raw data		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C142663		The original information, collected from the primary source.	OK	Unprocessed data (i.e. unnormalised, prior to fourier transformation)
Compound		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C43366		A substance formed by chemical union of two or more elements or ingredients in definite proportion by weight.	OK	A chemical substance composed of two or more elements
Medium		http://purl.bioontology.org/ontology/npo#NPO_1853		A fluid which can hold other substances in solution or in suspension.	OK	The solute in which a sample is dilution or exposed to
Pore size		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C112332		A quantitative or qualitative measurement of the physical dimensions of the pores in a material.	OK	Diameter of pore
Speed		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C41146		A scalar measure of the rate of movement of the object expressed either as the distance travelled divided by the time taken (average speed) or the rate of change of position with respect to time at a particular point (instantaneous speed).	OK	Magnitude of velocity
Temperature		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C25206		A measure of the average kinetic energy of a system of particles. Temperature may be quantified, in the context of thermodynamics, as the potential of one system to transfer thermal energy to another system until both systems reach a state of thermal equilibrium.	OK	Degree of heat
Suspension		http://purl.bioontology.org/ontology/npo#NPO_532		A mixture in which fine particles are suspended in a fluid where they are supported by buoyancy.	OK	Heterogenous mixture of solids in solution with sufficient size to sediment but not dissolve in the solute
Extraction		http://purl.obolibrary.org/obo/CHMO_0001577		The transfer of a solute from a liquid phase to another immiscible or partially-miscible liquid phase in contact with it.	OK	The isolation of analytes from an undesiered matrix
Filtration		http://purl.obolibrary.org/obo/NCIT_C16583		The process of passing a liquid or gas through a filter.	OK	A mechanistic, biological or physical process by which solids are separated from liquids (or gases) by adding a barrier that only the fluid can pass through/that the solids of a defined size or property cannot
Freeze-drying		http://purl.obolibrary.org/obo/NCIT_C28150		A dehydration process typically used to preserve a perishable material. The specimen is frozen and then dehydrated at low temperature in a high vacuum.	OK	A low temperature, low pressure dehydraition technique
Freezing		http://purl.obolibrary.org/obo/NCIT_C48160		The act or event which causes the transition from a liquid to solid matter phase.	OK	Reducing the temperature of a liquid to the temperature at which its phase transforms from liquid to solid
Storage temperature		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C101707		The recommended storage temperature for a device.	OK	The optimal temperature at which samples should be stored (usually with the caveat of maximum time the sample is stable at given temperature); 2. Temperature an entity is stored at, mostly goes together with the storage conditions (e.g. stored dark at 4 degree C in a fridge)
Hydrophobicity		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C63813		The inherent characteristic of a molecule or substance to be immiscible in water. The property means that the moiety of interest does not dissolve in, absorb, or mix easily with water.	OK	A property of a molecule describing its propensity to associate with neutral or non-polar solvents or molecules as opposed to polar ones
Electrophoretic mobility		http://purl.bioontology.org/ontology/npo#NPO_1315		Mobility of a charged particle in electrophoresis, measured as the rate of migration (usually in cm/s) per unit electric field strength (usually V/cm) of the charged particle.	OK	Migration of analytes under an electric field through a conductive liquid
X-Ray photon spectroscopy		http://purl.obolibrary.org/obo/CHMO_0000404		Spectroscopy where the sample is illuminated with X-rays causing ionisation and the emission of photoelectrons, the energies of which are measured.	OK	Elemental and chemical state information about the surface of solid material sample. The incident x-rays cause photoelectrons to be emitted from the surface and the kinetic energy of these emitted electrons is characteristic of the element from which the photoelectron originated.
pH		http://purl.obolibrary.org/obo/UO_0000196		A dimensionless concentration notation which denotes the acidity of a solution in terms of activity of hydrogen ions (H+).	OK	An expression of acidity or basicity of a solution, defined as the concentration of hydrogen ions per litre
DLS intrument		http://purl.bioontology.org/ontology/npo#NPO_1766		An instrument which is used to perform dynamic light scattering technique.	OK	Particle sizing technique based on Brownian motion and scattered light
UV-Vis Spectrophotometer		http://purl.obolibrary.org/obo/ERO_0000895		A spectrophotometer which measures emissions in the ultraviolet-visible spectral region.	OK	Instrument to determine UV-Vis

Protocols Terms	Annotated in the admin interface	Ontology URL		BioPortal Description	Comparation Descriptions	Specialists Description
Cells		http://purl.obolibrary.org/obo/NCIT_C12508		The smallest units of living structure capable of independent existence, composed of a membrane-enclosed mass of protoplasm and containing a nucleus or nucleoid.	OK	The most basic biological unit of a living organism
Powder		http://purl.obolibrary.org/obo/NCIT_C45302		A solid substance in the form of tiny loose particles; a solid that has been pulverized.	OK	A dry bulf solid composed of fine particles
Laser induced breakdown detection		http://purl.obolibrary.org/obo/CHMO_0000258		A type of atomic emission spectrometry where a high energy laser pulse is used to generate a plasma which acts as the excitation source.	Missing Specialist	NA
Matrix-Assisted Laser Desorption/Ionization		http://purl.bioontology.org/ontology/CSP/4008-0064		soft ionization technique which produces quasimolecular ions of large organic molecules up to several 100 kDa molecular mass.	Missing Specialist	NA
Small-Angle X-ray Scattering		http://purl.obolibrary.org/obo/CHMO_0000204		A method for determining structure by measuring the change in direction or energy of X-rays scattered by a sample at low angles (0--10 deg.).	Missing Specialist	NA
Time of flight secondary ion mass spectrometry		http://purl.obolibrary.org/obo/CHMO_0000565		Mass spectrometry where the sample is bombarded with a stream of primary mass-selected particles and the secondary ions ejected from the sample are detected by accelerating them to the same (known) kinetic energy and measuring the time taken for each ion to reach a detector at a known distance. This time is dependent on the mass-to-charge ratio of the ion.	Missing Specialist	NA
Tip Enhanced Raman Scattering (nano-Raman)		http://purl.obolibrary.org/obo/CHMO_0000678		Spectroscopy where the Raman scattering of monochromatic light, from a visible laser (500--650 nm), by metal surfaces, where scattering is enhanced by the optical near-field of a metal-coated scanning probe microscopy tip, is detected.	Missing Specialist	NA
Wide-Angle X-ray Scattering		http://purl.obolibrary.org/obo/CHMO_0000207		A method for determining structure by measuring the change in direction or energy of X-rays scattered by a sample at wide angles (>10 deg.). Wide-angle X-ray scattering is used for determining the structure of polymers.	Missing Specialist	NA
Conductivity		http://purl.obolibrary.org/obo/NCIT_C134263		A measure of the ion-facilitated electron current through a material.	Missing Specialist	NA
Extractant		NA		NA	Missing Specialist	NA
Ionic strength		http://purl.obolibrary.org/obo/NCIT_C52478		The weighted concentration of ions in solutions.	Missing Specialist	NA
Purity (resistivity)		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C62352		A quantitative assessment of the homogeneity or uniformity of a mixture. Alternatively, purity refers to the degree of being free of contaminants or heterogeneous components.	Missing Specialist	NA
Viscosity		http://purl.obolibrary.org/obo/NCIT_C75912		The resistance of a liquid to sheer forces and flow.	Missing Specialist	NA
Limit of Quantification- must be added in KI! Or add "Lower limit of detection" to eNM?		http://purl.obolibrary.org/obo/CHMO_0002802		The smallest measure that can be quantified with reasonable certainty for a given analytical procedure.	Missing in KI	**Limit of quantification is the value which gives you the lowest, reliable quantifiable amount of a compound**
Upper limit of detection		NA		NA	Missing in BioPortal	The largest value measurable using a defined method
Dilution scale factor		NA		NA	Missing in BioPortal	The degree to which the concentration of a analyte has been reduced, **2. We only use dilution factor**
Dilution		???		NA	Missing in BioPortal	Reduction in concentration of an analyte
Milling		???		NA	Missing in BioPortal	The use of rotational cutting or grinding to reduce the size of a bulk material
Homoaggregation rate		NA		NA	Missing in BioPortal	The rate of the transfer of aggregates from the bin (size interval) of smaller particle size to the bin of larger particle size.
Particle shape		-			Missing in BioPortal	The geometric profile of a nanoparticle
Brunauer–Emmett–Teller analysis		see Methods sheet			Missing in BioPortal	Technique used to determine the surface area of solid particles
Energy Dispersive X-ray Spectroscopy in the SEM and TEM		see Methods sheet; not exactely- compound term			Missing in BioPortal	Chemical analysis method that relies on X-ray excitation of the sample
Nanoparticle Tracking Analysis		see Methods sheet; not exactely- compound term			Missing in BioPortal	Particle sizing technique based on Brownian motion and scattered light
Scanning Transmission Electron Microscope-Energy-dispersive X-ray spectroscopy		see Methods sheet; not exactely- compound term			Missing in BioPortal	Technique to provide elemental composition. A focused beam of electrons is formed that is scanned over the sample from the upper-left to lower-right pixels of a specimen while some desired signal is collected to form an image. STEM-EDX is STEM coupled with an EDX detector.

Protocols Terms	Annotated in the admin interface	Ontology URL		BioPortal Description	Comparation Descriptions	Specialists Description
Thermogravimetric analysis coupled with IR-GC or MS		see Methods sheet; not exactely- compound term			Missing in BioPortal	Samples can be heated under inert gas (N2) or pyrolysed (air) at selected temperatures to monitor the gases evolved. The infrared spectrometer is ideal for identifying CO2, while the GCMS is well suited to identify volatile organic compounds (VOCs)
Pipettes		http://localhost/plosthes.2017-1#7339		NA	Missing in BioPortal	Handheld equipment to precisly aliquot liquids; **2. They come in very different shapes with different levels of accuracy from single glass pipettes, to adjustable or even electronic and multichannel pipettes - it might be useful to always state the name and scale and level of accuracy together with the term pipette**
Cuvettes		http://id.loc.gov/authorities/subjects/sh85035015		NA	Missing in BioPortal	Receptical for liquids for spectrophometric analsysis; **2. Cuvettes is again a very divers term - describing them for different kind of applications (photometric, chemistry etc.) as well as being from very different materials (e.g. plastic, glass)**
Pipettors- perhaps erase it from KI		NA		NA	Missing in BioPortal	Synonym of pipette; **2. I had to look up the difference between pipette and pipettor (we don't use the latter)**
Malvern Zetasizer		NA		NA	Missing in BioPortal	Equipment to perform DLS and zeta potential analyses
Disposable cuvettes		must be added comp terms		NA	Missing in BioPortal	Non reusable cuvettes (Typically plastic rather than Quartz); 2. usually used for photometry (e.g. optical density reading) and consist of plastic
Calibrated Volume Pipettor- perhaps erase it from KI		must be added comp terms		NA	Missing in BioPortal	Synonym of pipette; **2. we do not use anything else than non calibrated pipettes (and we don't use the term pipettor)**
Aqueous liquid		See CompTrms			Missing in BioPortal	A solution in water (ammonium barcarbonate made up in water, as opposed to methanol)
Biological tissues		See CompTrms			Missing in BioPortal	A collections of cells and extracellular matrix from the same origin/organ that carry out a specific function; **2. tissue sample from any living being - always useful to state from which organism and organ**
Solid matrix		NA		NA	Missing in BioPortal	NA
CO2 concentration		NA		NA	Missing Both/Maybe not that important	NA
Chloride concentration		NA		NA	Missing Both/Maybe not that important	NA
Dissolved organic carbon/surfactants		NA		Na	Missing Both/Maybe not that important	NA
O2 concentration		NA		NA	Missing Both/Maybe not that important	NA
Other particles		NA		NA	Missing Both/Maybe not that important	NA
Phosphate concentration		NA		NA	Missing Both/Maybe not that important	NA
Preferential orientation		See CompTrms			Missing Both/Maybe not that important	NA
Water concentration		NA		NA	Missing Both/Maybe not that important	NA
Addition of chemicals		See CompTrms			Missing Both	NA, **2. We use 'spiking' instead of addition**
Density matching of fluid		See CompTrms			Missing Both	NA
Average size dimension		See CompTrms			Missing Both	NA
Deposition rate		See CompTrms			Missing Both	NA
Elemental composition and chemical purity		http://purl.enanomapper.org/onto/ENM_0000082, http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C62352			Missing Both	NA, 2. agree, and we give details of either the purity (e.g. 99 %) and/or what the impurities are (composition as well as percentage)

Protocols Terms	Annotated in the admin interface	Ontology URL		BioPortal Description	Comparation Descriptions	Specialists Description
NP-cell interaction		-		NA	Missing Both	NA
Redox speciation		-		NA	Missing Both	NA
Assay-on-a-chip		see Methods sheet			Missing Both	NA
Asymmetrical field flow fractionation		see Methods sheet			Missing Both	NA
Centrifugal Field-Flow Fractionation-MALS		see Methods sheet			Missing Both	NA
Centrifugal field flow fractionation		see Methods sheet			Missing Both	NA
Column test		see Methods sheet			Missing Both	NA
Dialysis + ICP-MS		see Methods sheet			Missing Both	NA
Disc centrifuge		see Methods sheet			Missing Both	NA
Dye loaded field flow fractionation		see Methods sheet			Missing Both	NA
Force tensiometry		see Methods sheet; not exactely- compound term			Missing Both	NA
Full field transmission X-ray microscopy		see Methods sheet; not exactely- compound term			Missing Both	NA
Hydrophobic interaction chromatography		http://localhost/plosthes.2017-1#1177		NA	Missing Both	NA
MALS/SLS		see Methods sheet; not exactely- compound term			Missing Both	NA
Mastersizer		NA		NA	Missing Both	NA
Nuclear magnetic resonance spectroscopy relaxation		see Methods sheet; not exactely- compound term			Missing Both	NA
Quartz crystal microbalance with dissipation monitoring		see Methods sheet; not exactely- compound term			Missing Both	NA
SEC/HDC/HIC		see Methods sheet; not exactely- compound term			Missing Both	NA
Scanning transmission X-ray microscopy		see Methods sheet; not exactely- compound term			Missing Both	NA
Single Particle Inductively Coupled Plasma Mass Spectrometry		see Methods sheet; not exactely- compound term			Missing Both	NA
Single Particle Time of flight Inductively Coupled Plasma Mass Spectrometry		see Methods sheet; not exactely- compound term			Missing Both	NA
Single-cell Single Particle Inductively Coupled Plasma Mass Spectrometry		see Methods sheet; not exactely- compound term			Missing Both	NA
Time resolved Dynamic Light Scattering		see Methods sheet; not exactely- compound term			Missing Both	NA
Time resolved Single Particle Inductively Coupled Plasma Mass Spectrometry		see Methods sheet; not exactely- compound term			Missing Both	NA
Time resolved nanoparticle tracking analysis		see Methods sheet; not exactely- compound term			Missing Both	NA
Ultracentrifugation + ICP-MS		see Methods sheet; not exactely- compound term			Missing Both	NA
Ultrafiltration + ICP-MS		see Methods sheet; not exactely- compound term			Missing Both	NA
X-Ray Diffraction - crystalline phase		see Methods sheet; not exactely- compound term			Missing Both	NA
X-Ray Diffraction - crystallite size		see Methods sheet; not exactely- compound term			Missing Both	NA
X-ray absorption near edge spectroscopy		see Methods sheet; not exactely- compound term			Missing Both	NA
Interfering components or isotope		See CompTrms			Missing Both	NA
Osmotic concentration		See CompTrms			Missing Both	NA
Phase		http://purl.bioontology.org/ontology/npo#NPO_1610		A substance or a portion of a substance, which has uniform physical and chemical properties.	A bit different	Distinctive state of a material such as solid, liquid, gas or plasma
Parameters		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C80474		Technical specifications about a device that are issued by the manufacturer.	A bit different	Characteristic defining or classifying factor for a particular system
Lowest limit of detection		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C105701		The smallest concentration of an analyte that can be determined with a stated precision or confidence.	A bit different	The smallest value measurable using a defined method; **2.Limit of quantification should be added, limit of detection is not quantitative but qualitative**
Amplitude		http://ncicb.nci.nih.gov/xml/owl/EVS/Thesaurus.owl#C70831		The magnitude of an oscillation.	A bit different	This is context dependant as there are several different "types" of amplitude
Transmission electron microscopy with electron energy loss spectroscopy		http://purl.obolibrary.org/obo/CHMO_0000373		Spectroscopy where a beam of electrons with a known, narrow range of kinetic energies is transmitted through a sample and the energy distribution of the transmitted electrons is measured.	A bit different	TEM coupled with an EELS detector. Electron energy loss spectroscopy (EELS) involves measuring energy loss dispersion of inelastically scattered high-energy electrons transmitted through a thin sample.