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SAbyNA

H2020-NMBP-15-2020

Simple, robust and cost-effective approaches to guide industry in the development of safer nanomaterials and nano-enabled products

Start date of the project: 01/03/2020

Duration 48 months

WP2 D2.1– Distillation of existing resources for exposure assessment of NFs/NEPs

WP	2	Streamlined methodologies, models and tools to facilite release, fate & exposure assessment of NFs/NEPS for SbD purposes	
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[1] Dissemination level: **PU** = Public, **PP** = Restricted to other programme participants (including the JU), **RE** = Restricted to a group specified by the consortium (including the JU), **CO** = Confidential, only for members of the consortium (including the JU)
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Deliverable abstract

The aim of Task 2.1 (T2.1) has been to distil existing data, methods, models and tools for the early estimation of release, fate and exposure for Safe by Design (SbD). This has been a three-fold activity and has been separated into resources for environmental release, fate and exposure; resources for human exposure; and data sources for human and environmental exposure.

Following the criteria selection in Milestone 2.1, seventeen models/tools were identified for environmental release and exposure and distilled. From this, five tools/models for exposure and three tools/models for release and grouping have been shortlisted for Task 2.2. These identified models/tools are generally not suited for SbD purposes. As part of Task 2.2, aspects of the shortlisted tools/models will be optimised for incorporation into GUIDEnano. There are limited nano-specific standards for environmental exposure. Thirteen methods, in which are five are nano-specific will be taken forward.

Eleven models/tools were identified for human exposure and the relevant information for these tools/models distilled. Six of these models/tools have been shortlisted for inclusion for optimising in Task 2.2. It was found, as per for environmental tools/models, no tool/model is generally suited for SbD purposes. The shortlisted tools/models will be optimised and incorporated into GUIDEnano as per the environmental tools/models. One identified gap is the lack of tools for dermal exposure; this will be kept under review for potential developments. Five methods for dustiness and sixteen methods for release & exposure and RMM assessment were identified. Two methods were subsequently excluded. These methods will be taken forward to Task 2.2.

Eighteen data sources for human and environmental exposure were shortlisted. Following the criteria defined in Milestone 2.1, this was reduced to eight data sources. Following distillation, three data sources have been identified to be taken forward. These are the eNanoMapper system, the NanoCommons platform and the MESOCOSM database management system.

Table of Content

0. Abbreviations

AFNOR	Association Française de Normalisation
API	Application Program Interface
ART	Advanced Reach Tool
BSI	British Standards Institute
CB	Control Banding
CEN	The European Committee for Standardisation
CNF	Carbon nanofibre
CNT	Carbon nanotube
DB	Database
DIN	Deutsches Institut für Normung e.V.
DoW	Description of Work
DSA	Data Sharing Agreements
EB	Exposure Band
ECHA	European Chemical Agency
EHS	Environment, Health and Safety
ENM	Engineered Nanomaterial
e-NM	eNanoMapper
FAIR	Findable, Accessible, Interoperable and Reusable
FF	Far field
FIOH	Finnish Institute for Occupational Health
GUI	Graphical User Interface
HSE	Health and Safety Executive
INRS	French National Research and Safety Institute for the Prevention of Occupational Accidents and Diseases
ISO	International Standardization Organization
KB	Knowledge
LCA	Life Cycle Assessment
MFA	Material Flow Analysis
NEA	Nano-Enabled Article
NEP	Nano-Enabled Product
NEM	Nano-Enabled Material
NF	Nanoform
NIOSH	The National Institute for Occupational Safety and Health
NM	Nanomaterial
NOAA	Nano-objects and their aggregates and agglomerates
NP	Nanoparticle
OECD	Organisation for Economic Co-operation and Development

OEL	Occupational Exposure Limit
PEC	Predicted Environmental Concentration
RA	Risk Assessment
RMM	Risk Mitigation Measure
SbD	Safer by Design
SME	Small and Medium Enterprise
SOP	Standard Operation Procedure
UNE	Spanish Association for Standardisation
WP	Work Package
WWTP	Waste Water Treatment Plant

1. Introduction

The first step in the SAbyNA project is the mapping and establishment of context and purpose of the most relevant existing resources that can support Safe By Design (SbD) of nanotechnology.

Task 2.1 builds upon recent work examining existing tools for release and exposure prediction at the different stages of the innovation process (e.g. NanoReg2, caLIBRAte). This deliverable builds upon the work presented in Milestone 1 which provided the criteria for the selection of methods, data, models and tools that would be distilled.

This deliverable describes the distillation of existing resources (data, methods, models and tools) for environmental and human release and exposure prediction. This document describes the resources selected based on the criteria presented in Milestone 1 and the results of the assessment process for the distillation process.

2. Description of the tasks

This deliverable is split into two parts with a separate section for data sources for human and environmental exposure:

- Part 1: Resources for environmental release, fate and exposure
- Part 2: Resources for human exposure

For both Part 1 and Part 2, similar tasks have been performed for the distillation of existing resources. The first sub-task related to the criteria for the selection of methods, data, models and tools presented in Milestone 1 with these selected based on the criteria. The next sub-tasks involved an assessment of the selected resources for human and environmental release and exposure for distillation. The final sub-task involved recommendations to be taken forward to Task 2.2.

Excel files have been built to organise the resources for environmental release, fate and exposure and human exposure. These are available at: https://drive.google.com/drive/folders/1Q0VRsWkocbPsLnAWSeMSf8HW-lLg5vSr

3. Part 1: Resources for environmental release, fate and exposure assessment

3.1 Criteria for the selection of existing resources

3.1.1 Models and tools

Environmental exposure assessment models and tools include those that estimate the material flow of nanomaterials, their transport, fate and chemical speciation in different environments, and to a lesser extent the uptake of nanomaterials by biota.

To select which models/tools we would consider for assessment, a number of include and exclude rules were devised. If models/tools did not meet this criteria, they were not carried forward to assessment.

Include:

1. **Models/tools that are implemented in a "ready to use format**" (e.g. web link, downloadable software or spreadsheet, free of charge, or otherwise freely available within the consortium). Capable of being supplied with predefined "standard" environmental scenarios would be useful, but will be assessed further in the criteria for optimisation. Exceptions are allowed if the model/tool is not currently available

but there are plans to make it available, or if algorithms used by the model are documented and of interest for incorporation into the SAbyNA Guidance Platform.

2. **Models/tools that are nano-specific**, i.e. that explicitly allow simulation of processes specific to nanomaterial environmental fate. At a minimum this should include:
   i. sticking/heteroaggregation to solid materials (soil solids, aquatic sediments);
   ii. transformation to a non-nanosized form (e.g. dissolution/degradation).

Nanomaterials behave significantly different in the environment to their non-nano counterparts, notably forming thermodynamically unstable suspensions, necessitating the use of nano-specific models. There are a significant number of nano-specific models and so including this as a criterion does not limit the scope of models that will be assessed.

Exclude:

1. **Closed-access, non transparent and poorly documented models** which would be difficult, impossible or costly to assess or optimise. Documentation (which can include published articles and instructions presented via a model/tool's UI) will be considered insufficient if it does nott, at a minimum, include enough information to be able to parameterise and run the model for a custom scenario, unless use of the tool is self-explanatory enough to not need specific documentation. Exceptions are allowed if the model/tool is still under development and documentation is a work in progress, as long as there is knowledge within the consortium to be able to use the model.

3.1.2 Methods

We took a similar include/exclude format for the selection of methods.

Include:

1. Methods to derive data required by the models and tools, notably parameters determining release and attachment efficiencies.
2. We will prioritise methods that have been standardised internationally (CEN/ISO) or at national level (BSI, AFNOR, DIN, UNE…) or methods for which there are guidelines by recognised institutions (OECD, national health & safety organisation (e.g. NIOSH, HSE, FIOH, INRS) or SOP developed in international or national projects.

Exclude:

1. Methods that are not structured and are not accepted by the scientific community. For instance this includes methods that are insufficiently documented (unpublished/proprietary), site specific, instrument specific, out-of-context standards, lacking basic characterisation requirements.

Availability of standardised nano-specific methods is limited, and so we will not constrain ourselves to nano-specific methods. However, preference will be given to either nano-specific methods, or methods which have guidance for adaptation to studying ENMs.

3.2 Criteria for the assessment of existing resources to be distilled

Resources that meet the selection criteria above will be further assessed to determine which go forward for optimisation (Task 2.2). The assessment criteria is more focussed than the selection criteria and has the goal of determining which resources (or elements of resources) are most suited to optimisation for SbD purposes.

3.2.1 Assessment of tools and models

The following considerations were used when performing the assessment of tools and models:

1. **Models must be multimedia**, unless a single-compartment model is of specific use when assessing a particular case study (e.g. a case study with potential environmental release only to surface waters).

2. **Ease of parameterisation** – how difficult are the model/tool or model algorithms to parameterise, has parameterisation already been performed for relevant scenarios? Difficulty in parameterisation is likely to arise from availability in relevant data.
3. **Model run time** – is the computational run time of the model/tool/algorithms reasonable for incorporation into the SAbyNA guidance platform? Bearing in mind that large geographical and temporal scenarios with long run times does not necessarily mean computationally expensive algorithms.
4. **Access to model code and ease to navigate** – for optimisation, the model/tool code must be accessible and navigable, such that key process algorithms can be identified and incorporated into the SAbyNA guidance platform. Considerations related to this include whether the model is open access, what programming language the model is written in (and whether it is a proprietary language), how well documented the model code is, and whether there is expertise within SAbyNA on using the model/tool.
5. **Assessment of model applicability to SAbyNA case studies** – is the model capable of modelling the SAbyNA case studies at present, or with simple modifications?
6. **Models of differing spatial resolution**. All exposure models to be capable of at least 'regional' (~100x100 km) PEC prediction and either capable of nesting a local scenario (~10 km or smaller) within a regional scenario, or to be capable of full spatial resolution of a regional scenario to 10km or smaller, and be capable of either.
7. **Models that are capable of either**:
    a. steady state prediction across multiple media;
    b. dynamic prediction across single or multiple media.
8. **Tools for which there are available data.**
9. We will prioritize **tools that use standardised terminology**.

As per the selection criteria, we will confirm that all exposure models include fate and transformation processes specifically designed for particulate materials (e.g. (hetero)aggregation kinetics), unless modification has been made to enable nano-specific modelling that enable the simulation of processes highlighted above.

3.2.2 Assessment of methods

The following considerations were used when performing the assessment of methods:

1. **Standards body**: Is the method an internationally recognised standard, and if so what standard body (ISO, OECD, CEN, etc.).
2. **Is the method nano-specific**, or is guidance available to make it nano-specific. We will give priority to methods that are nano-specific, but won't automatically exclude those that aren't.
3. **Output variables**: What is the main thing the method is measuring, and how does this relate to input data required by models/tools?
4. **Status – draft, published, concept**: Is the method published, in draft form, or still a work in progress. When is the method likely to be published?

Nano-specific methods are limited, and so it is unlikely that we will be presented with multiple methods to determine the same variable. However, if this occurs, considerations such as ease of implementation and how realistically the method simulates realistic environmental behaviour will be assessed.

3.3 Analysis of the distillation of resources

The assessment itself was implemented in a Google Sheets spreadsheet (e.g. Figure 1), with assessment criteria listed as columns and resources as the rows. We aimed for each resource to have at least two assessors, particularly for resources for which there was not already expertise within SAbyNA. The assessment was coordinated between environmental and human resources, and hazard resources in WP3, to ensure where there are overlaps in resources, effort was not duplicated.

3.3.1 Tools and models

Figure 1 shows an extract of the spreadsheet used to assess environmental release and exposure models/tools. In total, 17 models/tools were considered for selection, with one not meeting the selection criteria (Table 1).

	Description	Format	Access (open access, proprietary, etc) and ease to navigate	Documentation
NanoFASE model	Spatiotemporal multimedia NM fate, exposure and biouptake model.	Fortran source code, can be compiled to exe for use on Windows, Linux or Mac.	http://nanofase.eu/. Model will be open source (via GitHub) when release version completed. Code written in Fortran and reasonably well commented. Model developers (UKCEH) are in WP2 so navigating the code won't be an issue.	Sparsely documented, with full documentation in progress. Limited documentation not an issue for SAbyNA as model developers (UKCEH) are in WP2
SimpleBox4nano	Multi-compartment box model providing background PECs. Nano-specific version of regulatory tool SimpleBox.	Excel spreadsheet with some programmatic access via R. R package under development.	https://www.rivm.nl/en/soil-and-water/simplebox4nano. Free to use, access on request. Must gain permission to modify.	Reasonable documentation and spreadsheet is relatively self explanatory. UKCEH know the model quite well.
GUIDEnano	Web-based guidance tool to aid nano risk assessment, including assessment of human and environmental exposure.	web based	https://www.guidenano.eu/	A 1 hour video is available explaining the model as well as different report from the GUDEnano project and NanoCommons (D6.1 and D6.2) and articles.
NanoPHEAT	Predicts an estimated exposure to materials of interest and superimposes this effective dose onto endpoint-specific dose-response curves for a variety of nanomaterials.	web based	http://nikc.egr.duke.edu/#!/model/nanopheat; https://yt210.shinyapps.io/NanoPHEAT/	No user documentation
Adam et al, 2019 (MFA to predict releases)	Probabilistic MFA model to predict environmental releases of different forms (pristine, matrix-embedded, dissolved, transformed)	Unknown	Don't think the model is available openly	None available
TNO spatial release model	Predicts spatiotemporal releases of NM from MFA model outputs. Developed as part of NanoFASE project.	Unknown	Publication in progress. Not publically available (yet), but Sam has some of the data.	None available
MendNano	Dynamic multicompartmental model of environmental media and biota, implemented in user-friendly web-based GUI. Outputs PECs. Integrates with LearNano (there's an option to use LearNano to define releases).	Web based	https://nanoinfo.org/mendnano/	Demonstration video available: http://nanoinformatics.org/2012/webinar/mendnano

Figure 1. An extract of the spreadsheet used to assess environmental release and exposure models/tools

Table 1. Environmental release and exposure models/tools which were assessed. * denotes models which are not currently openly available but to which we have potential access within the consortium

Name	Type	Met selection criteria?
NanoFASE	Exposure	Yes*
SimpleBox4nano	Exposure	Yes
GUIDEnano	Release and exposure	Yes
NanoPHEAT	Hazard	No – exposure not predicted
Adam et al, 2019 (MFA to predict release)	Release	Yes*
TNO spatial release model	Release	Yes*
MendNano	Exposure	Yes
LearNano	Release	Yes
nanoFate	Exposure	Yes
NanoDUFLOW	Exposure	Yes*
Rhine model	Exposure	Yes*
Rhone model	Exposure	Yes*
WSM/WASP7	Exposure	Yes
SUN Decision Support System (SUNDS)	Release and exposure	Yes
NanoApp	Grouping	Yes
LICARA NanoSCAN	Release and exposure	Yes
GWAVA	Exposure	Yes

In general, the models/tools are not designed for SbD purposes and their use for this purpose, in their current format, is likely to be difficult. For example, most environmental fate models include a somewhat empirical conceptualisation of the physchem properties of ENMs (e.g. attachment efficiencies) which might not be detailed enough to incorporate small changes to product design. GUIDEnano is the most promising tool for SbD purposes. As such, we propose to shortlist models and identify elements that are particularly useful or that could be tailored for SbD purposes (e.g. algorithms, conceptualisations, scenarios), with a view to incorporating these into GUIDEnano. This shortlist was chosen based on: (i) the desire to have a range of model application "types"

– e.g. regulatory relevant (SimpleBox4nano), spatiotemporal multimedia (NanoFASE), with graphical interface (GUIDEnano); (ii) ruling out models which had similar process algorithms to more advanced models (e.g. the NanoFASE model uses the same surface water conceptualisation of NM as the Rhine/Rhone models).

This further assessment will happen in Task 2.2, and the shortlist of models is:

- Exposure:
    - NanoFASE – *one of the more advanced models in terms of geographical representation and NM conceptualisation*
    - SimpleBox4nano – *regulatory relevant, useful for calculating background concentrations and does not have an onerous number of landscape (geographical) settings*
    - GUIDEnano
    - MendNano – *unable to access website, but this model is probably most similar to GUIDEnano and so we will continue to check for access. Some information is available in literature*[4]
    - nanoFate – *interesting to explore further as this model was developed separately from many of the others, so may use different conceptualisations that could be useful*
- Release and grouping:
    - LearNano – *unable to access website, but we will continue to check for access*
    - NanoApp – *tool for grouping nanoforms for REACH registration purposes*
    - LICARA NanoSCAN – *will be updated soon so we will keep checking for progress*

Many models were developed consecutively and in consultation with previous model developers, and thus use similar NM conceptualisation and algorithms for fate processes. This was the main reason for exclusion – that useful elements from that particular model are already present in an included model (e.g. the NanoFASE model draws on many of the algorithms in the Rhone/Rhine river models).

The following is a discussion of areas for potential improvement.

Accessibility of models

Most models in Table 1 are not openly accessible, but we have access to them within the consortium. Some models will become open source in the near future (e.g. NanoFASE). We have prioritised models for improvement in Task 2.2 that are accessible (or will be accessible, i.e. NanoFASE), with the exception of nanoFate due to its interest as being distinct from other NM exposure models. As we are likely to be extracting certain algorithms/processes from models, the inaccessibility of nanoFate is not an issue as its processes and algorithms are well detailed in documentation. MendNano and LearNano are normally accessible but their website is down at the moment. These are of particular interest due to their similar positioning to GUIDEnano and SimpleBox4nano, and so we will continue to check for access.

Geographical considerations

Most models include some geographical representation of the environment and this will require careful consideration when applying models to SAbyNA case studies. Options for improvement could include the creation of a set of theoretical scenarios, e.g. release from one WWTP/factory and the subsequent downstream movement of ENMs. This has the benefit of massively reducing the input data requirements for many of the more geographically-based models (e.g. NanoFASE).

Model run times

Model run times are generally short (<1s) for models with no or limited spatiotemporal resolution. Long run times are mostly due to geographical models run over long time periods. The creation of simplified geographical

[4] Liu and Cohen, Environ. Sci. Technol. **48** 3281, *Multimedia Environmental Distribution of Engineered Nanomaterials* (2014).

scenarios will help this. The elements of models that we are likely to include in GUIDEnano are unlikely to have prohibitively large model run times, though if they do, improvements to this can be considered (e.g. different solving regimes for numerical equations).

Uncertainty and sensitivity analyses

Few environmental fate models have published uncertainty and/or sensitivity analyses. This is generally a complex task for environmental models due to the large number of input parameters, and the need to consider environmental heterogeneity (i.e. spatial and temporal differences in parameters) alongside parameter uncertainty (e.g. uncertainty in phys/chem parameters for ENMs). The former is particularly useful for simpler models with limited spatial/temporal resolution, allowing predictions that represent a distribution that is likely to be seen in the environment. We will explore the possibility of performing such analyses in Task 2.2.

Sensitivity analyses can be particularly useful in determining the critical ranges of input parameters – the values of those parameters between which small changes results in significant changes to model output (i.e. ENM concentrations). This gives crucial information on input parameters for SbD purposes. For example, if the likely range of an input parameter is outside of this critical range, then SbD measures which change this parameter slightly are likely to be ineffective at altering environmental exposure. Such information can be used at a screening level for assessing the effectiveness of SbD measures. Of the models assessed, this has only been published in detail for SimpleBox4nano[5]. However, an OECD Working Party on Manufactured Nanomaterials report on exposure models (currently in draft) has undertaken sensitivity analyses of a number of exposure models. Results from this and other previous work will be used and expanded on, where appropriate, in Task 2.2.

Availability of input parameters

Most models have only been applied to one or a few scenarios and materials, meaning input parameters are available for these scenarios but nothing else. Some input parameters which are relevant to SAbyNA case studies are available (e.g. TiO_2, Ag, ZnO), but there is very limited information on certain materials (e.g. carbon black). There is also very limited information on how SbD modifications to the materials relevant to case studies will effect their phys/chem input parameters. Assessing the potential for including sensible default parameters based on these and for other scenarios/materials is a clear choice for model improvement. They could include selecting realistic ranges for environmental parameters (e.g. river flows, suspended sediment concentrations, soil erosion rates), and default phys/chem parameters for well characterised materials.

3.3.2 Methods

Figure 1 shows an extract of the spreadsheet used to assess environmental methods. A variety of resources were assessed, from standards that focus on individual chemical transformations, to projects that focus on driving forward nano-specific standards development. We have primarily focussed on methods which will predict parameters for models/tools assessed, such as dissolution rates and attachment efficiencies. Internationally standardised methods are prioritised, though we acknowledge that a lack of standardisation of nano-specific methods means other robust methods with well-developed SOPs are considered.

[5] Meesters *et al.,* Environ. Sci.: Nano **6** 2049, *A model sensitivity analysis to determine the most important physicochemical properties driving environmental fate and exposure of engineered nanoparticles* (2019).

	Type (OECD/ISO etc)	Nano-specific?	Output variable(s)
TG 318: Dispersion Stability of Nanomaterials in Simulated Environmental Media	OECD TG	Y	Dispersion stability (function of agglomeration and sedimentation)
GD 318: Guidance Document for the testing and interpretation of data on dissolution rate and dispersion stability of nanomaterials for effects and exposure assessment	OECD GD	Y	Dispersion stability and dissolution rate
TG 105: Water solubility	OECD TG	N	Aqueous dissolution rate
GD 29: Guidance Document on transformation/dissolution of metals and metal compounds in aqueous media	OECD GD	N	Aqueous dissolution/transformation rate
WNT project 3.10: TG on Dissolution Rate of Nanomaterials in Aquatic Environment	OECD WNT project	Y	Aqueous dissolution rate
WNT project 1.5: Determination of Solubility and Dissolution Rate of Nanomaterials in Water and Relevant Synthetic Biological Media	OECD WNT project	Y	Aqueous and biological dissolution rate
WNT TG programme project 3.16: Guidance Document Environmental abiotic transformation of nanomaterials	OECD WNT project	Y	Aqueous transformation rate
WNT project 3.14: Guidance Document to support implementation of TG 312 for Nanomaterial Safety Testing	OECD WNT project	Y	Soil leaching

Figure 2. An extract of the spreadsheet used to assess environmental methods

In general, there are limited nano-specific standards, but this is currently an active area of research, for example through the OECD Joint WNT/WMN Expert Group on Physical Chemical Properties of Nanomaterials. Table 2 lists standards relevant to environmental release and exposure, and Table 3 shows working groups and projects currently working on nano-specific standards development.

Table 2. Environmental release and exposure relevant methods

Name	Nano-specific
OECD TG 318: Dispersion stability of nanomaterials in simulated environmental media	Yes
OECD GD 318: Guidance Document for the testing and interpretation of data on dissolution rate and dispersion stability of nanomaterials for effects and exposure assessment	Yes
OECD TG 105: Water solubility	No
OECD GD 29: Guidance Document on transformation/dissolution of metals and metal compounds in aqueous media	No
ISO 19057: Nanotechnologies — Use and application of acellular in vitro tests and methodologies to assess nanomaterial biodurability	Yes
OECD TG 312: Leaching in Soil Columns	No
EN ISO 7784-1: Paints and varnishes - Determination of resistance to abrasion - Part 1 : rotating abrasive-paper-covered wheel method	No
EN ISO 11507: Paints and varnishes - Exposure of coatings to artificial weathering - Exposure to fluorescent UV and water	No
EN ISO 16474: Paints and vanishes - Methods of exposure to laboratory light sources	No
The EPA standard Method 1311; 167 Toxicity Characteristic Leaching Procedure	No
ISO 4892-2:2013 plastics - Methods of exposure to laboratory light sources	No
ISO 21683:2019 Pigments and extruders – Determination of experimentally simulated nano-object release from paints, varnishes and pigmented plastics	Yes
EU H2020 NanoREg SOP: Development of an aquatic Mesocosms Platform allowing the evaluation of kinetics of aggregation. *Nanoreg Public Deliverable D3.05*. 2016.	Yes

Name	Nano-specific
Available online: https://www.rivm.nl/en/documenten/nanoreg-d3-05-dr-development-of-aquatic-mesocosms-platform (accessed on 31 July 2019).	

Table 3. Projects currently working on nano-specific standards development

Name
OECD WNT project 3.10: TG on Dissolution Rate of Nanomaterials in Aquatic Environment
OECD WNT project 1.5: Determination of Solubility and Dissolution Rate of Nanomaterials in Water and Relevant Synthetic Biological Media
OECD WNT project 3.16: Guidance Document Environmental abiotic transformation of nanomaterials
OECD WNT project 3.14: Guidance Document to support implementation of TG 312 for Nanomaterial Safety Testing
EU H2020 project NanoHarmony
EU H2020 project NanoReg2 – *project has finished and initial work under its umbrella has been taken over by other projects*

Limiting ourselves to nano-specific and recognised standards (e.g. OECD, ISO) only would limit the selection of available methods. Hence, we will take forward all methods to Task 2.2, where we will map them to input parameters required by models/tools. We will also continue to monitor evolving work such as those projects listed in Table 3.

It is promising that most of the important parameters required by exposure models (e.g. dissolution rates, attachment efficiencies, those related to release) are represented, though there is clear ongoing work to improve these.

Future work will include a more detailed assessment of these methods, including theassessment of the potential for their improvement in Task 2.2. We will also explore whether new/improved methods from project partners with relevant experimental expertise can be considered for inclusion into the SAbyNA Guidance Platform.

4. Part 2: Resources for human exposure

4.1 Criteria for the selection of existing resources to be distilled

4.1.1 Models and Tools

Human exposure models and tools include inhalation and non-nano specific dermal models for workers and consumers. Most of the development has been within inhalation exposure in occupational settings, for which there is a variety of models and tools (e.g. Nanosafer, GUIDEnano) and control banding tools (e.g. CB NanoTool, Stoffenmanager nano). However, dermal exposure or consumer exposure is less developed.

To select which models/tools we would consider for assessment, a number of include and exclude rules were devised. If models/tools did not meet this criteria, they were not carried forward to assessment.

Include:

1. **Inhalation exposure models/tools in occupational settings:** At a minimum, these should be currently available for use for occupational exposure. This should include:
    i. Nano-specific models in a ready to use format.
    ii. ART (Advanced Reach Tool)
2. **Inhalation exposure of consumers**, i.e. which allows simulation of processes specific for consumer exposure. This is particularly relevant for the SAbyNA paints case study. This should include:
    i. Nano-specific models implemented or not in a ready to use format
3. **Dermal exposure i.e. that** allow simulation of processes specific to dermal exposure for occupational settings and/or consumers. This should include:
    i. Generic models that could be adapted to NFs, implemented or not in a ready to use format
4. **Either qualitative or quantitative models**

Exclude:

1. **Generic (non-nano-specific) inhalation exposure models.** There are a number of nano-specific models available for inhalation exposure, so this does not limit the number of models to be assessed.
2. **Sector specific dermal models not relevant for SABYNA (e.g. for solvents)**
3. **Models/tools reported in peer-review literature but that would be difficult to implement in a ready to use format.** This would be difficult or costly to asses and optimise. The published literature may also contain insufficient information for running the model for scenarios (such as the SAbyNA case studies), insufficient information on the parameters and on the algorithms used.

4.1.2 Methods

A similar approach has been used for selecting methods. The inclusion/exclusion criteria are as follows:

Include:

1. Methods to derive data required by the models and tools. For example the parameters required for exposure assessments and measurements.
2. We will prioritize methods that have been standardised internationally (CEN/ISO) or at national level (BSI, AFNOR, DIN, UNE…) or methods for which there are guidelines by recognised institutions (OECD, national health & safety organisation (e.g. NIOSH, HSE, FIOH, INRS) or SOP developed in international or national projects.

Exclude:

1. Methods that are not structured and are not accepted by the scientific community. For example, this includes methods that are insufficiently documented (unpublished/proprietary), out-of-context standards, lacking basic characterisation requirements and not recognised by the community.

4.2 Criteria for the assessment of resources to be distilled

4.2.1 Assessment of models and tools

A number of assessment criteria has been selected for the distillation of models and tools for human exposure in the Excel file (illustrated in Table 3). The criteria used for the assessment are the following:

- **Relevant use of the tool and model (Safer NM/Safer production/Safer use)**. This is to determine the relevant use of the tool and model. For Safer NM, the options are divided into human hazard, human RA, Environmental hazard, and Environmental RA. Safer production is divided into worker exposure, worker risk, and process safety. Safer use is divided into consumer exposure, consumer RA, and release from products.

- **Expertise required**. Options are beginner, intermediate, and advanced/expert. A separate column is also used for any specialised expertise required, for example specific computer skills and experience in performing risk assessments. Expertise is important to consider as the targeted end user are SMEs.
- **Applicability.** Possible options are general (i.e. the tool/model is non-specific) or the tool/model is for a specific NF or a specific exposure scenario.
- **Type of tool and model.** Possible options are control banding, risk screening, life cycle assessment, framework, numerical estimate values, database, guidance document, guidance tool, and other.
- **Output type.** Options are qualitative, quantitative, and semi-quantitative. Specific outputs from exposure assessment tools can include exposure bands, exposure classes and exposure potential (i.e. low/medium/high exposure potential).
- **Exposure route.** Possible routes that the tool/model can cover, these are inhalation, dermal, and oral.
- **Link to model/tool**
- **Spatial resolution for exposure.** This considers the emission source and the receptor. Options are personal, near field, or far field.
- **Time to run the model and tool**. This concerns the time which is required for the user to input the relevant data and the time that the model/tool takes to process the data and supply a result. The possible options included in the Excel spreadsheet are 1-10 minutes, 11-30 minutes, >30 minutes <1 hour, >hour, day, or >day.
- **Assessment of performance**. This concerns if the tool includes a scenario that can be run by the user to assess is the user is using the tool correctly (i.e. using the correct input information). There is also a tab to describe if the tool has been assessed in another source (i.e. European projects such as caLIBRAte, publications, and other reports)
- **Stage gate.** Level the tool has been ranked at according to Stage Gate (Gates 1-6).
- **Model assumptions.** Description of the assumptions the model presumes for inputs and outputs (i.e. physical state of the nanomaterial, benefit/risk is assessed).
- **Input required from the user.** Description of the input parameters that are required to be entered by the user.
- **Availability of input parameters**. High, medium or low. There is also a separate tab in the Excel spreadsheet which indicates the input parameters required for each tool/model.
- **Inter-user variability**. For a given scenario, if two people use the tool is there variability in the results and what is the extent of the variability. A SAbyNA case study has been performed by two different users for each tool.
- **Demonstration with ‘real life’ scenarios**. Has the tool been validated with measurement data and/or validated with a ‘real life’ scenario.
- **Regulatory acceptance.** This concerns if the tool/model been accepted by ECHA or other regulatory authorities.
- **Limitations.** Description of documented limitations and/or any limitations observed during the assessment.
- **Scenario/use best for the tool and model**. Description on the best use for the tool/methods (i.e. for the two SAbyNA case studies, there is a need to include paints and 3D printing).
- **Uncertainty**. Description on how the tool deals with uncertainty (i.e. model uncertainty, parameter uncertainty, and scenario uncertainty).
- **Possible improvements**. These findings will be used in Task 2.2. This includes suggestions on what could be more precise and reliable, potential improvements to the algorithms, additional and better described input parameters, and potential strategies to reduce the uncertainty.
- **Tool/model updated on a regular/periodic basis**. Assessment if the tool is being updated/maintained (Yes/No).
- **Contribution to SbD**. Assessment on aspects of the tool/models which could be utilised for SbD.

4.2.2 Assessment of methods

A number of assessment criteria has been selected for the distillation of methods for human exposure in the Excel file (as illustrated in Figure 3). The criteria used for the assessment are the following:

- **Parameter/method output**. For the assessment, this has been divided into dustiness and exposure & release assessment and RMMs.
- **Title**. Method title.
- **Source/code reference**. Number of the method.
- **Link**. Web address for where the method can be found.
- **Description**. Summary of the purpose of the method
- **Method Tier**. The options are Tier 1 (initial assessment), Tier 2 (basic assessment), and Tier 3 (comprehensive assessment) as reported in ISO 17058.
- **Level of standardisation**. Method standardisation- standardised internationally (CEN/ISO) or at national level (i.e. BSI, AFNOR, DIN, UE) or guidelines by recognised institutions (OECD, national health & safety organisation (e.g. NIOSH, HSE, FIOH, INRS).
- **Output variables**. The outputs of the method (e.g. dustiness ratings, particle concentration).
- **Uncertainty of the method**. Discussion of uncertainties described in the method and/or from the review.
- **Limitations**. Discussion of potential limitations of the method to be taken into consideration.
- **Other comments**. Other relevant aspects that may be beneficial in the assessment.
- **Input parameters**. This tab is linked to the input parameters of the assessed tools/models. The purpose of this is to select methods that are required for the inputs for the models and tools.

4.3 Analysis of the distillation of resources

Using the selection criteria for tools and models (section 4.2.1) and methods (section 4.2.2), a number of tools and models and methods have been distilled for human exposure. These are discussed in the following sections.

4.3.1 Tools and models

An example of the assessment for the tools and models is illustrated in Figure 3. Eleven tools and models were assessed with nine considered to be relevant (Table 4. . The ANSES CB Tool for NMs was not considered as this tool is not publically available. NanoRiskCat after review was also excluded as it is not suitable as it is not a tool but is similar to a database.

Tool	Description	Format	Expertise required	Specialised expertise required i.e.	Applicability	Type of tool
Precautionary Matrix	The precautionary matrix helps to assess the need for nanospecific	Web-based and desktop	Intermediate	Some RA experience	General	Risk Screening
ANSES CB Tool for NMs	The control banding tool requires input data, irrespective of the phase of	Not available online	Intermediate	Unclear. If hazard "very high" or	Specific NF or scenario	Control
Control Banding Tool	The tool estimates an emission probability (without considering exposure controls) and severity band and provides advice on engineering controls to use to prevent exposure. It deals with occupational exposures, including nine domains covering	Excel sheet	Intermediate	Basic RA experience	Specific NF or scenario	Control banding
Stoffenmanager Nano	The tool estimate a hazard band and exposure band that are combined in	Word export report	Intermediate	Some RA experience and ability to	Specific NF or scenario	Control
Nanosafer CB	Online control banding and risk management tool for manufactured NMs.	PDF export report	Intermediate	Some RA experience and ability to	Specific NF or scenario	Control
ConsExpo Nano Tool	This tool can be used to estimate inhalation exposure to NMs in consumer	Online	Advanced/Expert	Expertise in the field	Specific NF or scenario	Risk Screening
SUNDS	The Sustainable Nanotechnologies Project Decision Support System: SUNDS	Web-based	Intermediate	RA experience; for tier 1 need some	General	Risk Screening
Guidenano tool	The tool guides the user (the nano-enabled product developers (industry)	Web-based	Advanced/Expert		General	Guidance tool
Licara NanoScan	The main goal of LICARA is to develop a structured life cycle approach for nanomaterials which enables the evaluation of the benefits and risks qualitatively with low and manageable efforts, over the nanoproduct's life time. It further allows a comparison with the risks and benefits of the conventional (non-nano) products. The tool stimulates economic, environmental and social opportunities. This tool is specifically intended for use by SME's to support them in communicating with regulators, and potential clients and investors.	Web-based	Intermediate		General	Guidance tool
ART	ART is a free web-based tool for the estimation of inhalation exposure at	Web-based	Advanced/Expert	RA knowledge and understanding	Specific NF or scenario	Numerical

Figure 3. Excel file for tools and models assessment

Table 4. Inhalation tools

Name	Met Selection Criteria?
Precautionary Matrix for NMs	Yes
Anses CB Tool for NMs	No (not available)
Control Banding Tool	Yes
Stoffenmanager Nano	Yes
Nanosafer CB	Yes
NanoRiskCat	No
SUNDS	Yes
GUIDEnano	Yes
Licara NanoScan	Yes
ART	Yes
ConsExpo Nano	Yes

From the distillation process, no one tool or model is generally suited for the requirements of SbD. For example, changes to the process (such as addition of other exposure controls or changes to the design) cannot be made directly into the models. For changing the process, the user would have to re-run the scenario implementing these changes. Many of the tools and models require an intermediate or advanced knowledge i.e. risk assessment experience and a detailed understanding of exposure data. These tools were also not initially developed for SbD purposes, but as control banding tools for implementing control measures or for prioritising risk measures to rank activities by their risk.

We propose to further review a shortlist of tools from the distillation and further identify usability improvements for aspects of these models that could be tailored (i.e. algorithms, input parameters, uncertainty etc.) and incorporate them into GUIDEnano. This shortlist has been chosen based on: (i) Tools and models which are regulatory relevant (e.g. Stoffenmanager Nano, ART) with graphical interfaces (e.g. GUIDEnano) (ii) ones which can be used as part of Part 1 of the SAbyNA platform as a quick check (e.g. Precautionary Matrix for NMs) (iii) ones in which the availability of parameters is "high" (e.g. NanoSafer CB, ConsExpo Nano, SUNDS, GUIDEnano, ART) (iv) ones which cover consumer exposure, the whole life cycle and the SAbyNA case studies (e.g ConsExpo Nano and SUNDS).

The shortlist of tools and models to be further considered in Task 2.2 include:

- Swiss Precautionary Matrix
- Control Banding Tool
- Nanosafer CB
- Stoffenmanger Nano
- ConsExpo Nano
- GUIDEnano
- SUNDS
- ART (not nano specific)

Tools and models which will not be considered at this stage are:

- ANSES CB Tool. This tool has not been included in the shortlist as there are issues for access;
- LICARA NanoScan. There are issues at the moment for access. This will be further reviewed in due course as it is understood this is being updated at the time of this review.

For the case studies, ConsExpo Nano is relevant for the paints sector. Existing tools and models will need to be streamlined into GUIDEnano for occupational exposure in the paints sector and tailored for additive manufacturing exposure assessment for 3D printing.

Areas where improvement could occur are discussed in the following sections.

Dermal Exposure

Dermal exposure is a gap in the tools and models currently available and will need to be investigated further. There are no nano-specific dermal tools and models openly available, this will be monitored through the project in case of potential developments currently in progress. Some of the tools and models consider dermal exposure, but not in any depth of detail.

A dermal version of ART (dART) is under development and may be available in due course. DREAM, which is a semi-quantitative dermal exposure tool is not available. Risk of Derm is publically available and has been assessed, although it is not nano-specific. The tool can be used for a number of predefined scenarios (filling, mixing or loading, spraying, dispersion and mechanical treatment). The inputs are qualitative only. The output is potential dermal exposure for hands exposure exclusively with median and percentile distributions per minute and for a shift.

Consumer Exposure

ConsExpo Nano is a tool which models exposure to nanomaterials for consumers in consumer spray products. Whereas some other tools and models consider consumer, but not in great depth, ConsExpo Nano is focussed on consumer inhalation exposure. The algorithms are precise, however this tool requires advanced RA experience. The output also requires advanced knowledge for interpreting if there is an exposure risk and to what extent. This tool is relevant for the paints case study within SAbyNA.

SUNDS is a tool which allows decisions for assessing and managing risks for nanoenabled products through their lifecycle, including for consumer exposure. SUNDS consists of two tiers, with Tier 1 requiring knowledge of Stoffenmanger Nano and is based on LICARA Nanoscan and Tier 2 being based on the REACH authorisation process. The tool requires intermediate knowledge for risk assessment and knowledge of Stoffenmanager Nano.

Model Assumptions

From the distillation, information on the assumptions for the models and tools is limited. One aspect that could be improved, where this information is available is the assumptions. For example, it is known that the Precautionary Matrix assumes there are no protective measures in place, the CB tool assumes there are some engineering measures in place (although this is not taken into account for the risk level output), ConsExpo Nano assumes a spraying distance and ART is based on two shifts. No model assumptions are available for Stoffenmanager Nano. This is the only information for model assumptions.

In order to improve the usability, the assumptions will be investigated further as part of T2.2.

Input parameters

As part of the distillation process, the input parameters for each model have been collated as described in the online Excel sheet. Examples of input parameters requested by models for exposure include parameters including dustiness, emission rate, room volume and ventilation type/rate. The model will require all the input parameters to be entered by the user. For input parameters we have also used the caLIBRAte deliverable “D7.1 Mapping of input requirements and data formats for the tools” along with the related annexes.

Table 5. Examples of input parameters

Model	Phys-Chem parameters	Activity parameters	Exposure Factor parameters	Exposure Control parameters
Precautionary Matrix for NMs	Size	Activity Name	Amount, frequency	N/A
Stoffenmanager Nano	Size, shape	Process domain, activity name, weight fraction, production rate	Amount, room volume, duration, frequency, OEL	Ventilation type
GUIDEnano	Density, dustiness, size, shape, surface area	Mass %, amount, duration, frequency	Room size (width, height, length, volume, area), OELs	Ventilation rate

From the resources (such as documentation) available from the models, it can be unclear if the model uses all the input parameters. This is a major gap that we will investigate further in Task 2.2. As an example GUIDEnano requires the user to input a value for dustiness, however dustiness is not considered in the emission calculation.

Another feature for the input parameters is how the model reacts to changes on the input parameters relevant for SbD where precise information is required for the parameterisation. For example, does the model differentiate between particle sizes of 10 nm and 50 nm. Related to this, the Precautionary Matrix only ask the user if nano-relevance is based on the EU definition (2011/696/EU) or according to the precautionary approach (primary particles having external dimensions). Changing the particle size has no effect in Stoffenmanager Nano.

Another area that could be investigated is how a SbD tool would ideally allow a user to input information for the key exposure parameters with an uncertainty value if possible. After this process, the existing tools would then be measured against criteria for an ideal SbD tool. The results would then be used to identify areas of improvements.

Relevant SbD parameters that will need to be considered in this context include dustiness and exposure factor parameters (i.e. amount used, room characteristics, near field/far field). Potential improvements/additions to these parameters can also be considered. This includes the ability to see in real time the impact of changing a parameter for best informing SbD strategies as early as possible in the innovation process.

Inter-user variability

As part of the distillation process, inter-user variability has been assessed using a SWCNT case study (Table 6). This involved one reviewer from IOM and one reviewer from LEITAT performing this on each distilled tool and model. Information was supplied on the activities (weighing and mixing) and available phys-chem properties of the SWCNTs for the case study. Inter-user variability is a factor which also needs to be considered as a source of uncertainty. It was not possible to perform the inter-user variability on SUNDS (due to usability issues), GUIDEnano (insufficient information for the mass balance model) and LICARA NanoScan (access currently unavailable).

Table 6. Inter-user variability

Name	Results (user 1)	Results (user 2)	Differences in Results
Precautionary Matrix for NMs	Worker: Va= 75 Consumers: Vawc=82	Worker: Va =66 Consumers: Va=75 and Vawc= 66	Difference in worker and consumer risks, however the output is "further investigation is needed"
Control Banding Tool	Severity band: high; Probability band: likely; overall risk level without controls: RL3 (Containment)	Severity band: Very high, Probability band: Likely, Overall risk: RL4, seek specialist advice	Difference in one RL band
Stoffenmanager Nano	hazard - E; exposure class 2, risk score 1 (weighing); as before except exposure class 1 (mixing)	Weighing (task weighted: hazard class E, exposure class 2, risk score 1; Mixing (task weighted: hazard class E, exposure class 2, risk score 1;	No difference
Nanosafer CB	EB5 & R5 for NF acute and daily and FF acute with EB2/R4 (FF daily) - mixing once a day. All EB5/R5 if 7 times a day	Weighing (NF acute: low potential, NF daily: very low potential, FF acute: very low potential, FF daily: very low potential); Mixing (NF acute: very high exposure, NF daily: high potential, FF acute: moderate potential, FF daily: very low potential)	Some differences in potentials
ConsExpo Nano Tool	Inhaled dose per event: Mass 1.2 × 10^{-3} mg)	Weighing (Inhaled dose per event: Mass 2.1 × 10^{-2} mg), Mixing (Inhaled dose per event: Mass 4.2 × 10^{-2} mg)	Differences in inhaled dose mass

Some differences have been observed between two different users in the assessed tools and models apart from Stoffenmanager Nano. For the other tools and models, there are differences in the results. In the Precautionary Matrix, there is a difference between the workers and consumers risk, although results above 20 are banded in one category which is for future investigation. In the Control Banding Tool, there is a difference in one band (between the two highest bands). In NanoSafer CB, this is the tool with the biggest differences for weighing, with one low risk potential and the other resulting in potentially high exposure potential. Mixing for both case studies in NanoSafer CB resulted in high exposure potential. In ConsExpo Nano, differences were also observed between users.

The differences in tools and model may be due to a number of factors. This includes assumptions used by the user for the activity such as in NanoSafer CB, the use of different options for inputs in the Precautionary Matrix and the Control Banding Tool and the use of different default scenarios in ConsExpo Nano. For some of the tools, the example scenario also did not contain all the required input information require, so operator interpretation was required. This will also affect the results.

The inter-user variability results in increased uncertainties, which is not as much of an issue for Stoffenmanger Nano from the inter-user variability case study. This analysis from inter-user variability can be used for proving more precise guidelines for how to input data for those parameters that are identified as having the highest inter-user variability.

The inclusion of a “check” scenario that can be used for the user to compare their results when running this scenario will be investigated. This would allow the user to see how they are interpreting the parameters. A note of caution is this “check” scenario would need to be done well and with careful thought to ensure there is no possibility of additional confusion. The user in this case may also not be an expert in the field, so consideration of this will also need to be taken into account.

Model Algorithms

Model algorithms may be an area in which selected algorithms could be used and improved where appropriate. However, in a number of cases this information is not available such as for Stoffenmanager Nano or limited in scope such as for LICARA NanoScan, Where available specific algorithms will be identified and assessed for improvement for incorporation into GUIDEnano, for example information us supplied on the algorithms used in the Precautionary Matrix in the guidelines.

Uncertainty

Uncertainty is an aspect which needs to be improved in the current tools and models (Table 7). ECHA have considered uncertainty as part of chemical safety assessments. ECHA list three types of uncertainty (ECHA, 2012)[6]:

- Model uncertainty – relating to simplifications the model makes;
- Parameter uncertainty – relating to individual model parameters/values/measurements;
- Scenario uncertainty – user dependent.

Table 7. Uncertainty in distilled tools and models

Name	Uncertainty considered
Precautionary Matrix for NMs	Considered as part of available information parameters
Control Banding Tool	"Unknown factors" are assigned score of 75% of high
Stoffenmanager Nano	Unclear
Nanosafer CB	Unclear
ConsExpo Nano	Monte Carlo
SUNDS	Monte-Carlo with 10 000 trials
GUIDEnano	Only for hazard- use multipliers
LICARA NanoScan	Based on number of unknown answers

It can be observed from the results of the inter-user variability, that there will be uncertainty in the scenario uncertainty between different tools and operators. Model uncertainty will be linked to model assumptions which needs to be considered as part of Task 2.2. Parameter uncertainty will also be investigated during Task 2.2 for the key parameters of the shortlisted tools and models use. Key parameters in terms of their importance to uncertainty will be identified and investigated. Sensitivity analysis from caLIBRate will also be considered. Methods for improving uncertainty may also be available to improve uncertainty such as Monte Carlo.

4.3.2 GUIDEnano considerations

There are a number of considerations that need to be taken into account for GUIDEnano. GUIDEnano has been selected for improvements, as the tool is the most promising for SbD purposes; it is the most promising tool for

[6] ECHA (2012). Guidance on information requirements and chemical safety assessment. Chapter R.19: Uncertainty analysis. https://echa.europa.eu/documents/10162/13632/information_requirements_r19_en.pdf

exposure and uses a graphical interface. GUIDEnano uses a numerical model rather than a mechanistic approach with a scoring system, which is used in control banding tools and Stoffenmanager Nano. The tool is also sensitive to small changes to input parameters, which makes it the most suitable tool for SbD purposes. Using GUIDEnano will also allow the development of modules for the two SAbyNA case studies for the paint and 3D printing sectors.

The tool uses a mass balance model to estimate exposure concentration in the near field and far field. To do so it requires quantitative information on the emission rate from the user (which may not be available). One drawback, is the tool requires more precise information that may not be available in the earlier stages of the innovation process. This precise information for the two SAbyNA case studies (paints and 3D printing) will be supplied by the project.

For setting the activity, the user must enter data on the dimension of the room where the activity take place, on the ventilation, and on the duration and frequency of the activity. For estimating worker exposure, the user must enter information on the time spent in the Near Field (FF) and Far Field (FF) and needs to enter information of the engineering controls in place and PPE eventually worn.

4.3.3 Methods

The methods of interest to SAbyNA are those that can be used for SbD purposes, those that can be used for the paints and 3D printing case studies, and those can be used to predict occupational and consumer exposure in the innovation process, including at early stages of the innovation process. The methods also need to generate data that can be used by the shortlisted tools and models. For WP2, the methods of relevance are those for dustiness and those for release/exposure assessments for exposure to NFs. The methods are discussed in the following sections and further information is available in the online Excel file (discussed in section 2).

An example of the assessment for the methods is illustrated in Figure 4. The methods have been divided into two separate categories (see Table 9 at the end of the methods section):

- Methods for dustiness. It is worth noting that there are a number of methods for dustiness. These can be incorporated into the SAbyNA platform with the user selecting the most appropriate method to use depending on user factors such as instrumentation and expertise in a particular method.
- Methods for release & exposure assessment and RMMs. Similarly to methods for dustiness, different methods for release & exposure measurement will be incorporated into the platform with improvements included from Task 2.2.

Parameter /method output	Title	Source/Code reference	Link	Description	Level of standardization	Output variables	Uncertainty of method
Release & Exposure Assessment - carbon black and amorphous silica	Nanotechnologies — Method to quantify air concentrations of carbon black and amorphous	ISO/DTS 21361:2019	https://www.iso.org/standard/70760.html	This document provides guidelines to quantify and identify air concentration (number of particles/cm3) of particles of carbon black and/or	ISO (international)	Air concentration (number of particles/cm3) by size	The following uncertainties are discussed in the standard:
Release & Exposure Assessment - Dermal exposure	Assessment of dermal exposure to nano-objects and their aggregates and agglomerates	CEN ISO/TS 21623:2018	https://www.iso.org/standard/71272.html	This document provides an overview for mechanisms of occupational dermal exposure to nano-enabled products or nanoparticles. This	ISO (international)	Risk assessment evaluation for potential for exposure based on	None stated in the document. May be some uncertainty with the data
Release & Exposure Assessment- Assessment of inhalation exposure	Workplace exposure – Assessment of exposure by inhalation of nano-objects and their aggregates and agglomerates	EN 17058:2018	https://shop.bsigroup.com/ProductDetail?pid=000000000030337090	Document outlines a measurement strategy for workplace exposure assessment when operating with NOAA. Outlines monitoring and sample collection options and the strategy to determine the exposure levels in various workplace zones (e.g. far field, near field etc.) and scenarios prior, during and after an activity to determine exposure and persistence for either basic, specific activity or comprehensive assessment.	ISO (international)	Direct reading count and particle size, with static sample collection for chemical or microscopy analysis.	Not stated in standard but will be specific to each manufactures direct reading instruments and off line detection techniques.
Release & Exposure Assessment- Guidance Framework-OEL	Nanotechnologies – Overview of available frameworks for the development of occupational exposure limits and bands for	ISO/TR 18637:2016	https://www.iso.org/standard/63096.html	Provides an overview of the available methods and procedures available in the development of Occupational Exposure Limits (OELs) and Occupational Exposure Bands (OEBs) for nano	ISO (international)	Guidance on: OEB/Hazard banding; control banding (exposure band and hazard band); provides	Use of uncertainty factors is discussed: simple, default approach often used to derive an OEL
Release & Exposure Assessment- Guidance Framework-Risk	Nanotechnologies – Occupational risk management applied to engineered	ISO/TS 12901-1:2012	https://www.iso.org/obp/ui/#iso:std:iso:ts:12901:-1:ed-1:v1:en	ISO/TS 12901:2012 provides guidance on occupational health and safety measures relating to engineered nanomaterials, including the use	ISO (international)	The size and density of the NPs should be employed as	Lack of standardization for fibrous nanomaterials measurements. Need for

Figure 4. Excel file for methods assessment

Methods for dustiness

The purpose of dustiness tests are to to simulate typical powder processing and handling in order to enable a comparison of the relative dust release potential of different bulk materials under a selection of controlled conditions to measure the aerosolised release. During testing particles are dispersed into the air and are described quantitatively, however no single dustiness method is likely to represent and reproduce the various types of processing and handling scenarios used in the workplace, hence the standard guides the user to choose the correct test required. Therefore, there are a number of methods for the design of dustiness devices and different values will be obtained by different test methods. Each of the dustiness methods measure the dustiness of bulk materials containing NOAA in terms of health related dustiness mass fraction, number-based dustiness index and number-based emission rate. In addition, it establishes test methods that characterize the aerosol from its particle size distribution and the morphology and chemical composition of its particles. The data generated can be used as an input value in some modelling tools to predict exposure e.g. dustiness data can provide the manufacturers of nanomaterials with information that can help to improve their products (e.g. by selecting less dusty nanomaterials) or the users to improve their processes or their technical prevention approaches.

Five methods have been identified for relevance for dustiness as listed in Table 9. These are EN 17199-1: 2019, EN 17199-2:2019, EN 17199-3:2019, EN 17199-4:2019 and EN 17199-5:2019. These methods are all ISO standardised. The following input parameters linked to model inputs are required by these methods: dustiness index, density, size, shape, diameter, particle number, particle concentration, particle size distribution, amount used (for testing), room temperature, humidity, duration (testing duration of the data collection), mass percent and physical state. There are a number of model input parameters not covered by the method, such as room dimensions and ventilation. The output from these methods are dustiness ratings in mg/kg (mass-based dustiness index) and/or particle/mg (number-based dustiness index).

Uncertainty of the methods is not described in the method; however there will be uncertainty associated with either the calculated or manufacturer uncertainty data. As part of Task 2.2., the vortex shaker method (EN 17199-5:2019) will be optimised.

Methods for release & exposure assessment and RMMs

The purpose of release & exposure assessment and RMMs methods are to determine the potential of exposure and release of NFs and RMMs that could be used. This can include assessing exposure by the inhalation and dermal routes of exposure and assessing by setting (occupational and consumer settings). There are a number of available methods which can be used dependent on the needs of the user for performing an assessment. For example methods can include checking that exposure levels comply with occupational exposure limits for the NF, assigning a control banding level, assessing RMMs used and also for developing strategies for measuring release and exposure.

Twelve methods have been identified as being relevant for the release and exposure assessment for nanoforms and nanoenabled products. Of these, eleven are relevant for inhalation exposure with one being relevant for dermal exposure. All of these methods have an international level of standardisation (ISO and EN). The model input parameters and method output variables are listed in Table 8). As can be observed, the methods generally only either consider a limited number of input parameters or consider a wide number such as ISO/TS 12901-1:2012.

Uncertainty for the methods is discussed in a number of methods and this is generally for uncertainties with instrumentation/measurement (EN 17058:2018), data uncertainties (i.e. ISO/TR 18637:2016 and ISO/TS 12901-2:2014), the extrapolation of data and inter-individual variability (NIOSH bulletin 63). One specific uncertainty listed in ISO/TS 12901-2014 is the lack of standardisation for measuring exposure to fibrous nanomaterials.

As part of Task 2.2, relevant methods for the case studies will be optimised depending on the experiments to be performed. It may be the case, that other methods may be added and adapted as the WP develops. The method outputs will also be investigated further i.e. if the output is a risk banding or quantitative output.

Table 8. Parameters for release & exposure assessment and RMMs methods

Method	Input parameters	Method Outputs
Nanotechnologies — Method to quantify air concentrations of carbon black and amorphous silica in the nanoparticle size range in a mixed dust manufacturing environment (ISO/DTS 21361:2019)	Size, particle size distribution, particle concentration	Air concentration (number of particles/cm^3) Carbon black Amorphous SiO_2 amorphous
Assessment of dermal exposure to nano-objects and their aggregates and agglomerates (NOAA) (CEN ISO/TS 21623:2018)	Size, state (‘high hazard' NOAA, flexible/non-rigid NOAA, liquid Nano-scale droplets and all other NOAA))	Risk assessment evaluation
Workplace exposure – Assessment of exposure by inhalation of nano-objects and their aggregates and agglomerates (EN 17058:2018)	Size, particle number, particle concentration, amount used, amount handled, amount in product, air exchange rate, frequency, spray duration, OEL, exposure controls	Direct reading count and particle size
Nanotechnologies – Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs) (ISO/TR 18637:2016)	Size, duration, OEL, ventilation type, ventilation rate	Control banding guidance
Nanotechnologies – Occupational risk management applied to engineered nanomaterials - Part 1: Principles and approaches (ISO/TS 12901-1:2012)	Density, surface area, size, shape, particle number, particle concentration, particle size distribution, air exchange rate, duration, frequency, employees exposed, OEL, exposure controls	Size and density for deriving exposure limits. Guidance on occupational health and safety for engineered nanomaterials

Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 2: Use of the control banding approach (ISO/TS 12901-2:2012)	Dustiness, size, particle size concentration, amount used, amount handled, room characteristics, ventilation rate, local controls	Control banding for inhalation exposure
Nanotechnologies – Health and safety practices in occupational settings (ISO/TR 12885:2018)	Dustiness, density, surface area, size, shape, particle number, particle concentration, particle size distribution, amount used, amount handles, amount in products, air exchange rate, OEL, exposure controls	Description of health and safety practices in occupational settings. Focus on occupational manufacture and use of manufactured NMs
Nanomaterials. Quantification of nano-object release from powders by generation of aerosols (CEN ISO/TS 12025:2015)	Dustiness, density, size, shape, particle number, amount used	Nano-object number release, nano-object release rate, nano-object aerosol number concentration, mass specific nano-object number release
Nanotechnologies - Nanomaterial risk evaluation (ISO/TR 13121:2011)	Density, surface area, size, particle number, particle concentration, particle size distribution, amount used, ventilation type, engineering controls	Guidance for risk evaluation and risk management
Characterisation of ultrafine aerosols/nanoaerosols- Determination of the size distribution and number concentration using differential electrical mobility analysing systems (ISO 28439:2011)	Surface area, particle number	Aerosol size distribution (number concentration distribution)
Workplace exposure - Measurement of exposure by inhalation of nano-objects and their aggregates and agglomerates - Metrics to be used such as number concentration, surface area concentration and mass concentration (EN 16966:2018)	Surface area, particle number, amount used, amount handled, physical state of matrix	Aerosol mass, number concentration
Workplace atmospheres — Ultrafine, nanoparticle and nano-structured aerosols — Inhalation exposure characterization and assessment (ISO/TR 27628:2007)	Surface area, size, shape, particle number, amount used, amount handled,	NOAA metric (calculated or estimated)
Occupational Exposure to Carbon Nanotubes and Nanofibres (NIOSH bulletin 65)	Worker respirable sample, OEL	Recommended exposure limit, worker exposure level
Occupational Exposure to Titanium Dioxide (NIOSH bulletin 63)	Personal sample, OEL	Recommended exposure limit, worker exposure level

Conclusion from the distillation process

Overall from the distillation process, the EN and ISO methods (listed in Table 9 below as meeting the selection criteria) will be investigated further in Task 2.2. Limiting the methods at this stage would only limit the selection of available methods in the platform. The two guidance documents, NIOSH bulletins 63 and 65 may be useful for guidance documents.

The following methods have been shortlisted from the distillation to be investigated further for improvements in Task 2.2:

- Dustiness: Measurement of dustiness of bulk materials that contain or release respirable NOAA or other respirable particles – Parts 1-5 (EN 17199-1:2019, EN 17199-2:2019, EN 17199-3:2019, EN 17199-4:2019 and EN 17199-5:2019)
- Release & Exposure Assessment and RMM Methods: ISO/DTS 21361:2019, CEN ISO/TS 21623:2018, EN 17058:2018, ISO/TR 18637:2016, ISO/TS 12901-1:2012, ISO/TS 12902-2:2012, ISO/TR 12885:2018, CEN ISO/TS 120252018, ISO 28439:2011, EN 16966:2018 and ISO/TR 27628:2007.

It may also be the case depending on the experiments to be performed, that additional methods may need to be added at a later point of the project and will be reviewed as part of the ongoing WP2 tasks. In terms of potential improvements, this could include changing variables and improving the uncertainty of the method. The methods also only generally cover a limited number of the input parameters required by the models and tools. Discussions will be undertaken with WP6 for how the methods will be used within the platform, for example will the platform guide the user to relevant methods, which could be performed. Information on instrumentation has also been distilled and is available by accessing the link in section 2.

Table 9. Assessed and shortlisted methods

Title	Reference	Met Selection Criteria?
Dustiness methods		
Measurement of dustiness of bulk materials that contain or release respirable NOAA and other respirable particles - Part 1: Requirements and choice of test methods	EN 17199-1:2019	Yes
Measurement of dustiness of bulk materials that contain or release respirable NOAA or other respirable particles - Part 2: Rotating drum method	EN 17199-2:2019	Yes
Measurement of dustiness of bulk materials that contain or release respirable NOAA or other respirable particles - Part 3: Continuous drop method	EN 17199-3:2019	Yes
Measurement of dustiness of bulk materials that contain or release respirable NOAA or other respirable particles - Part 4: Small rotating drum method	EN 17199-4:2019	Yes
Measurement of dustiness of bulk materials that contain or release respirable NOAA or other respirable particles - Part 5: Vortex shaker method	EN 17199-5:2019	Yes
Release & Exposure Assessments and RMMs Methods		

Title	Reference	Met Selection Criteria?
Nanotechnologies — Method to quantify air concentrations of carbon black and amorphous silica in the nanoparticle size range in a mixed dust manufacturing environment	ISO/DTS 21361:2019	Yes
Assessment of dermal exposure to nano-objects and their aggregates and agglomerates (NOAA)	CEN ISO/TS 21623:2018	Yes
Workplace exposure – Assessment of exposure by inhalation of nano-objects and their aggregates and agglomerates	EN 17058:2018	Yes
Nanotechnologies – Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs)	ISO/TR 18637:2016	Yes
Nanotechnologies – Occupational risk management applied to engineered nanomaterials - Part 1: Principles and approaches	ISO/TS 12901-1:2012	Yes
Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 2: Use of the control banding approach	ISO/TS 12902-2:2012	Yes
Nanotechnologies – Health and safety practices in occupational settings	ISO/TR 12885:2018	Yes
Nanomaterials. Quantification of nano-object release from powders by generation of aerosols	CEN ISO/TS 12025:2015	Yes
Evaluation of methods for assessing the release of nanomaterials from commercial, nanomaterial containing polymer composites	ISO/DTR 22293	No- standard currently under development
Pigments and extenders — Determination of experimentally simulated nano-object release from paints, varnishes and pigmented plastics	ISO 21683:2019	No- relevant for environmental exposure
Nanotechnologies - Nanomaterial risk evaluation	ISO/TR 13121:2011	Yes
Occupational Exposure to Carbon Nanotubes and Nanofibres	NIOSH bulletin 65	Yes
Occupational Exposure to Titanium Dioxide	NIOSH bulletin 63	Yes
Characterisation of ultrafine aerosols/nanoaerosols- Determination of the size distribution and number concentration using differential electrical mobility analysing systems	ISO 28439:2011	Yes

Title	Reference	Met Selection Criteria?
Workplace exposure - Measurement of exposure by inhalation of nano-objects and their aggregates and agglomerates - Metrics to be used such as number concentration, surface area concentration and mass concentration	EN 16966:2018	Yes
Workplace atmospheres — Ultrafine, nanoparticle and nano-structured aerosols — Inhalation exposure characterization and assessment	ISO/TR 27628:2007	Yes

5. Data sources for human and environment exposure

This section describes the distillation and assessment of existing data sources for the environmental release, fate and exposure and human exposure data. This process involved the selection of data sources based on the criteria presented in Milestone 2.1 and the results of the assessment performed for the distillation process. The criteria used for the selection and distillation process is detailed in the section 5.1.

5.1 Criteria for selection of existing data sources

To select which data sources will be considered for the assessment, we identified and prepared an extensive list of data sources available from many completed and ongoing EU sponsored (FP7 & H2020) and Non-EU projects. The full list of data sources is provided in the Annex 8.1. This list included data platforms with datasets from many different projects, individual project databases and knowledge-based resources. This work benefited from the similar resource sheets produced in the PROSAFE and GRACIOUS projects. To distil the data sources, a number of include and exclude rules were devised for the assessment. If data sources did not meet this criteria, they were not carried forward to the assessment process.

Include:

- **Data sources which include relevant data for human and environmental release, fate and exposure:** A comprehensive list of data sources was established from various available EU sponsored and Non-EU projects, which included data for phys-chem characterisation, toxicology, ecotoxicology and environmental exposure. Only the relevant data sources with release, fate and exposure data for the WP2 assessments were selected.
- **Database presence:** It was certain from the project website or known through the working knowledge of the partners that release, fate and exposure data is generated, made available and stored in a properly structured and normalised database.

Exclude:

- Many projects and data sources were excluded from the list due to not having the relevant release, fate and exposure data required for the WP2 assessment.
- If it was not certain that a proper database has been produced by a project then it was excluded from the list.

Based on the selection criteria provided above, we short-listed the following data sources which were further assessed and distilled in the next task.

Table 10. Shortlisted data sources

Project Title	Website	Comments
GUIDEnano	www.guidenano.eu	Exposure Scenario Data (Workers: 196, Service Life: 4); Web-based Risk Assessment Tool; ecotox data;
MARINA	http://www.marina-fp7.eu/	Phys-Chem 14 materials; In-vitro (8 cells types, 10 assay types, 209 Tests); In-vivo (8 Tests); Eco-tox data (40 Tests); Omics (Proteomics: 52 (substance x cell type x timepoint combinations), Metabolomics: 52 , Transcriptomics: 24); Exposure Scenario Data (Workers: 55, Service Life: 4); Most MARINA data transferred to e-NM instance (share with CALIBRATE & Nanoreg2);
NanoFase	http://nanofase.eu/	Phys-Chem, EcoTox, exposure; Models; Possible data sharing? - DSA req;
NanoMICEX	http://www.nanomicex.eu	Possible phys-chem, some ecotox & exposure data;
NANoREG	http://www.nanoreg.eu/	NanoReg 1 data publicly available in e-NM DB; phys chem, invitro & in vivo tox, ecotox, exposure; phys chem and tox templates
NanoReg2	http://www.nanoreg2.eu/	NanoReg 2 data accumulating in e-NM DB instance; phys chem, invitro & in vivo tox, ecotox, exposure. Sources data from NANoReg, MARINA, Nanotex, ENPRA and Nanogenotox.
SANOWORK	http://www.sanowork.eu	Limited in-vitro results
SUN	http://www.sun-fp7.eu	Phys-Chem 8 materials; In-vitro (2 cells, 4 assay types, 17 Tests); In-vivo (9 Tests); Eco-tox data (205 Tests); Omics (Yes); Exposure Scenario Data (96 from NECID); Environment, Release Exposure (28 Datasets);
Dana	http://www.nanoobjects.info/en/nanoinfo/knowledge-base	KB - Searchable for nano materials containing products
OECD Database on Research into the Safety of Manufactured NMs	http://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm	Publications in the Series on the Safety of Manufactured Nanomaterials
NECID	http://www.perosh.eu/research-projects/perosh-projects/necid/	NECID (Nano Exposure and Contextual Information Database) by PEROSH group; Database system for detailed nano-exposure data and measurements; potential tool for

		use and as source of data from other projects
ENPRA	http://www.enpra.eu/	Phys-Chem 12 materials; In-vitro (24 cells, 58 assay types, 650 Tests); In-vivo (17 Tests); IVIVE (83 Tests); Toxico-Kinetic Data (Yes) ; Exposure Modelling Data (Yes);
CALIBRATE	http://www.nanocalibrate.eu	Develop, integrate and validate models; sourcing data from other projects (eg MARINA); Modelling and Exposure information; continue to relate and poss data sharing agreements (DSAs)
MESOCOSM	https://aliayadi.github.io/MESOCOSM-database/	The first centralized mesocosm database management system for environmental nanosafety containing experimental data collected from mesocosm experiments suited for understanding and quantifying both the environmental hazard and exposure.
BIORIMA	https://www.biorima.eu/	Started Noc 2017; ENM Phys-chem, in-vitro, in-vivo, ecotox; tox modelling; RMM toolbox establish relations and poss DSAs
NanoCommons	https://cordis.europa.eu/project/rcn/212586_en.html	Research and Innovation action to support networking & development: Joint Research Activities will integrate existing resources and organise efficient curation, preservation and facilitate access to data/models.
eNanoMapper	https://enanomapper.net/	Platform for EHS data repository; being adopted and used in Gracious and other projects (CALIBRATE, NanoReg 1 & 2, etc)
GRACIOUS	https://www.h2020gracious.eu/	eNanoMapper DB established and data population ongoing
NICK	http://nikc.egr.duke.edu/	Largely literature data, but also NanoFASE project data being incorporated via Nanocommons.

5.2 Criteria for assessment of data sources to be distilled

Data sources that met the initial selection criteria were further assessed to determine which go forward for the data optimisation in Task 2.2. The assessment criteria in this process was more focussed than the initial selection criteria and had the goal of determining which data sources and elements of data sources will be suitable for the assessment and optimisation purpose.

The following considerations were made while performing the further assessment of data sources:

- **Data accessibility:** Data sources which were available online through cloud platforms and easily accessible with clear guidance available to search, filter, link and extract the data. We also included data sources which could be used without the user guidance e.g. which could be used with the help of partners who were familiar or were involved in the project.
- **Published data:** Data sources that includes publically and freely available data, which could be openly accessed without any data embargoes or restrictions
- **Standardised Data:** Data sources that contains data which has been collected and stored in some sort of standardised and harmonised fashion with the use of ontologies or standard terminologies
- **Curated Data:** Data sources which contains data that has been properly curated with the known source, meta data and classifications
- **FAIR Data:** Data that has been made available (or in progress of making) using the FAIR principles (by making it findable, accessible, interoperable and reusable)
- **Applicability to SAbyNA case studies:** Data that is relevant for SAbyNA case studies
- **Availability through SAbyNA partners:** Data that is available through the SAbyNA partner connections who already have access to data or connections with the data providers
- **Data from data platforms:** Data in process of publication or already available on data platforms e.g. NanoFASE and NanoMile data through the NanoCommons platform

We excluded the data sources which:

- Does not have relevant data for the SAbyNA Platform
- Are not easily accessible, not published or currently are under data embargos and restrictions
- Does not include data that has been standardised with the use of ontologies
- Does not include data that has been properly curated (i.e. the data has gone a process where their validity has been checked with those who generated the data, is free of errors and properly organised in a readable format).

Taking into consideration the above selection criteria in Task 2.1, we further shortlisted the data sources as listed in Table 11:

Table 11. Further shortlist of data sources

Project Title	Website	Comments
GUIDEnano	www.guidenano.eu	Exposure Scenario Data (Workers: 196, Service Life: 4); Web-based Risk Assessment Tool; ecotox data;
MARINA	http://www.marina-fp7.eu/	Phys-Chem 14 materials; In-vitro (8 cells types, 10 assay types, 209 Tests); In-vivo (8 Tests); Eco-tox data (40 Tests); Omics (Proteomics: 52 (substance x cell type x timepoint combinations), Metabolomics: 52 , Transcriptomics: 24); Exposure Scenario Data (Workers: 55,

		Service Life: 4); Most MARINA data transferred to e-NM instance (share with CALIBRATE & Nanoreg2);
NanoFase	http://nanofase.eu/	Phys-Chem, EcoTox, exposure; Models; Possible data sharing? - DSA request;
CALIBRATE	http://www.nanocalibrate.eu	Develop, integrate and validate models; sourcing data from other projects (eg MARINA); Modelling and Exposure information; continue to relate and poss data sharing agreements (DSAs)
NanoCommons	https://cordis.europa.eu/project/rcn/212586_en.html	Research and Innovation action to support networking & development: Joint Research Activities will integrate existing resources and organise efficient curation, preservation and facilitate access to data/models.
eNanoMapper	https://enanomapper.net/	Platform for EHS data repository; being adopted and used in Gracious and other projects (CALIBRATE, NanoReg 1 & 2, etc.)
GRACIOUS	https://www.h2020gracious.eu/	eNanoMapper DB established and data population ongoing;
MESOCOSM	https://aliayadi.github.io/MESOCOSM-database/	The first centralized mesocosm database management system for environmental nanosafety containing experimental data collected from mesocosm experiments suited for understanding and quantifying both the environmental hazard and exposure.
NICK	http://nikc.egr.duke.edu/	Largely literature data, but also NanoFASE project data being incorporated to via Nanocommons.

All of the data sources listed above have either made or in process of making data available through the eNanoMapper or NanoCommons platform. Some of the projects data on both of these platforms is publically available, and some is under embargo. Hence, we will mainly focus on testing the SAbyNA case studies and providing suggestions for improvement primarily on these two platforms; which will cover most of the data sources selected during the selection process. This work will hugely benefit by having access to the eNanoMapper database and NanoCommons platform through previous projects involvement, working knowledge, open access to some data and good connections with the SAbyNA partners. Another data source that was selected for assessment is the MESOCOSM database. For the case studies testing, the entire process flow (from start to end) will be followed; which will highlight any potential issues and gaps in the data sources. These will be reported with the suggestions for improvement in the Task 2.2.

5.3 Analysis of the distillation of data sources

This task aimed to assess the current usability of distilled data sources from Task 2.1. The information presented here is not meant to be used for directly accessing the available data, but as a compass for understanding the nature of the data sources/platforms and their features. The assessment was synchronised with hazard data sources assessment task in WP3, to avoid duplicating the efforts where there are overlaps.

The following parameters were assessed for the data source evaluation:

- Project Title/Data Source
- Web Access
- Available Data Types
- Guidance Documentation Available
- Publically Available
- Standardised/Use of Ontology
- Data Collection Methods (e.g. standardised templates)
- Data Output Formats (e.g. excel, xml, json etc.)
- Support for Analysis/Modelling
- Allows API (e.g. link to models or Jupyter)
- Data Quality Criteria
- Is Data Curated (e.g. annotated)
- Is Data FAIR (findable, accessible, interoperable and reusable)
- Any Limitations Noted

Assessment findings of the three selected data platforms (eNanoMapper, NanoCommons and MESOCOSM) are given in the following sections.

5.3.1 Project Title/Data Source: eNanoMapper system

The eNanoMapper system was developed as part of EU sponsored FP7 project (grant agreement no: 604134) to establish a community agreed ontology, databases system and modelling platform to support various domains of nanotechnology. Its use is being effectively mandated by the EU Project Officers to help standardise and harmonise ongoing Nano-EHS research data storage efforts.

The eNanoMapper system has in the last few years become the de-facto principal data repository for many recently completed and currently ongoing nano projects. Each project is set up as a database “instance” that encapsulates the project’s users and their permissions to access one or more project datasets. eNanoMapper platform facilities (via its interfaces) federated search and retrieval capabilities across different projects throughout the platform. Each contributing project’s dataset forms a discrete unit of data, and access to (one or more) projects is granted on a project by project basis, depending possibly on data-sharing agreements, etc.

Web Access: https://search.data.enanomapper.net/

Available Data Types: eNanoMapper system supports storage of nanomaterials characterization data, biological and toxicological information. More recently, advancements has been made to store the human and environmental release, fate, exposure and OMICS data.

Guidance Documentation Available: eNanoMapper system provides a user-friendly HTML user guidance interface, as well as tailored interface to each database instance.

Publically Available: Currently, not much human exposure and environmental release, fate and exposure data is publically available due to project data embargos. However, the SAbyNA partners will have access to some of this data due to involvement in the projects.

Standardised/Use of Ontology: The eNanoMapper team has developed an ontology; which includes and defines common vocabulary terms in use in nano safety research with a classification hierarchy and other relationships.

Data Collection Methods (e.g. standardised templates): Standardised templates have been developed as part of GRACIOUS project. These templates are aligned with the GRACIOUS release and exposure ontology developments, which are implemented within the eNanoMapper database.

Data Output Formats (e.g. Excel, XMI, JSON etc): Users can download data from the user interface in a variety of formats and through a predefined selection of queries or the combination of queries, and data categories. Once the selection is made, this can be downloaded in 5 different formats: JSON, CSV, TXT, XML, or XLSX.

Support for Data Analysis and Modelling: In terms of extracting data for analysis and modelling purposes, eNanoMapper offers a widened variety of formats for downloading data, or its extraction via the API. In the general user interface the Export functionality is used to save selected data in one of the five available formats, i.e. json, txt, csv, xml or xslx, the exact options offered depending upon the complexity of the retrieval and structure of the resulting dataset. For example a simple table in a "flat" csv dataset may meet certain report and output format needs, but not the more complex dataset structures requiring the much greater flexibility of XML or JSON. The JSON format is always available and is the recommend format to be used for data analysis purposes.

Allows API (e.g. link to models or Jupyter): Application Programming Interface (API), which can be used to directly retrieve data into other packages and systems, e.g. to retrieve data into processing and analysis by other programs or packages such as Jupyter, or to feed data into a running model, etc. Beyond the collation of useful information regarding experiments undertaken by the studies collected, eNanoMapper offers the means to browse and compare data availability, for example across related experiments. The special "for developers" section gives the opportunity to search and download a series of information by using programming tools (via AMBIT REST web services with free text & faceted search API), for general analysis, data embedding or visualisation purposes, as well as to build data pipelines to meet the needs of more specific modelling. In addition, programmatic data access is critical for true data interoperability and is one of the most important FAIR requirements. It needs to be accompanied by adequate metadata that facilitates accurate and efficient interrogation of the data: The first FAIR criteria, Findable, requires metadata and data to be easy to find for both humans and computers. Machine-readable metadata are essential for the automated discovery of datasets and services, and the eNanoMapper REST API is an essential component of the FAIR data resource.

Data Quality Criteria: This is taking place alongside discussions and implementation of release and exposure data templates developed by GRACIOUS project.

Is Data Curated (e.g. Annotated): eNanoMapper is actively making advancement in the proper data curation aspects including the annotation and meta-data information of the data uploaded.

Is Data FAIR (findable, accessible, interoperable and reusable): Database is currently being actively developed to ensure conformance with the guiding principles of FAIR data (https://www.go-fair.org/fair-principles/), and also to enhance its data curation and data stewardship processes for FAIR data.

Any Limitations Noted: The main issue noted is the public accessibility of the release and exposure data. Most project data is under embargos. However great advancements have been made in terms of data standardisation and to make it FAIR. Further assessment will be done in Task 2.2 to test the SAbyNA case studies and suggestions for the improvement of usability will be provided.

5.3.2 Project Title/ Data Source: NanoCommons platform

NanoCommons is creating an e-infrastructure for enhancing data integration and to promote cross-field cooperation. It has developed a sustainable and openly accessible nanoinformatics framework (knowledgebase, integrated computational tools, data interpretation systems etc.) for assessment of the risks of NMs, their products and their formulations.

The NanoCommons project aims to provide an integrating platform for the NanoSafety community in Europe and globally. It is creating a FAIR data ecosystem guiding the users to the most appropriate solution that fits their needs, promotes data integration, sharing, enrichment and full data exploitation from their original source and ownership. It facilitates integrated approaches combining experiments, modelling and simulation processes.

Web Access: https://ssl.biomax.de/nanocommons/cgi/login_bioxm_portal.cgi

Available Data Types: NanoCommons system supports storage of nanomaterials characterization data, toxicological information, ecotoxicity, release, fate, exposure and OMICS datasets.

Guidance Documentation Available: NanoCommons system provides a user-friendly web-based user guidance interface to browse the knowledge infrastructure. It also provides an online user guidance handbook for nanoinformatics, data management, ontologies and workflows.

Publically Available: Some data from the closed projects is openly available. Other datasets which are still under embargo required to have data access and analysis agreement with the corresponding data owner (e.g. NanoFase).

Standardised/Use of Ontology: NanoCommons platform supports many ontologies e.g. eNanoMapper, NanoParticle, NCI, Gene etc.

Data Collection Methods (e.g. standardised templates): NanoCommons supports integration with the standardised templates developed by other nano projects for release, fate and exposure data e.g. NIKC/NanoFase and GRACIOUS.

Support for Analysis and Modelling: NanoCommons supports integration and federation of existing NMs data, interaction mechanisms, and knowledgebase and underpinning ontologies. It has developed a user-friendly interface for a suite of computational tools for mechanistic and statistical modelling, read-across, grouping, safe-by-design, life cycle assessment and benchmarking of their predictive power.

Data Quality Criteria: This system supports and provides protocols for the quality assurance criteria.

Data Curated (e.g. Annotated): It supports and provides guidance for data annotation, meta-data, general data management and curation aspects.

Is Data FAIR (findable, accessible, interoperable and reusable): NanoCommons infrastructure creates a FAIR data ecosystem guiding the users to the most appropriate solution that fits their needs; promotes data integration, sharing, enrichment and full data exploitation from their original source and ownership; facilitates integrated approaches combining experiment, modelling and simulation.

Any Limitations Noted: NanoCommons infrastructure aims to provide knowledge and tools for nano community including characterisation and control of data quality and uncertainty, development of data templates and workflow management tools, repository of protocols and associated metadata templates, knowledge infrastructure, data management, analysis and modelling tools, tool integration for risk assessment, grouping, read-across and risk assessment/decision tools. These are great advancements for SbD, however main limitation noted is the open accessibility of data, which is mostly under embargo or require data sharing agreements with the data provider. Further assessment will be done in Task 2.2 to test the SAbyNA case studies and suggestions for the improvement of usability will be provided.

5.3.3 Project Title/Data Source: MESOCOSM

This is the first centralized mesocosm database management system for environmental nano-safety containing experimental data collected from mesocosm experiments suited for understanding and quantifying both the environmental hazard and exposure. These entities are divided into different groups i.e. physicochemical properties of ENMs, environmental, exposure and hazard endpoints, and other general information about the mesocosm testing, resulting in more than forty parameters in the database. MESOCOSM aims to predict and explain ENMs behaviour and fate in different ecosystems as well as their potential impacts on the environment at different stages of the nano-products lifecycle. MESOCOSM is expected to benefit the nano-safety community by providing a continuous source of critical information and additional characterization factors for predicting ENMs interactions with the environment and their risks[7].

Database Setup: The database is available to all on the GitHub repository. Scientists and industries can visualize the totality or a part of the dataset, download the SQL database file and manipulate it with any database management system (Oracle, Postgres, MySQL, DB2 etc.), remotely interact with the database via an application program interface (API), or also download it with its application (graphical user interface) for local usage (on the local computer or server).

Web Access: https://aliayadi.github.io/MESOCOSM-database/

Supported Data Types: Contains 5200 entities covering tens of unique experiments investigating Ag, CeO_2, CuO, TiO_2-based ENMs as well as nano-enabled products. These entities are divided into different groups i.e. physicochemical properties of ENMs, environmental, exposure and hazard endpoints, and other general information about the mesocosm testing, resulting in more than forty parameters in the database.

Guidance Documentation Available: The MESOCOSM database provides its schema and logical database design online on the portal. It also provides online guidance on how to install and use the application.

Publically Available: MESOCOSM database and application is free to use under the licence agreement Creative Commons Share alike. The default license of MESOCOSM is Creative Commons (CC-BY 4) which allows users to download modify and reuse the data without restriction, but attribution of the source must accompany the reuse. MESOCOSM is also available as downloadable SQL file for free under an Open Database License v1.0.

Data Collection Methods (e.g. standardised templates): MESOCOSM is a distinct database resource providing thousands of experiment data obtained in tens of unique experiments investigating different nanomaterials based on results obtained within the H2020 projects. Its standardises the storage of environmental exposure and hazard data generated in database.

Data Output Formats/Visualisation (e.g. Excel, XMI, JSON etc): The MESOCOSM database is equipped with a powerful application, consisting of a graphical user interface (GUI), allowing users to manage and search data using complex queries without relying on programmers. A JAVA Graphical User Interface (GUI) is freely available to provide direct managing, searching and browsing. The web portal of the MESOCOSM database was built in HTML, CSS, JavaScript and JQuery to make it more attractive and user-friendly.

Allows API (e.g. link to models or Jupyter): It allows to remotely interact with the database via an application program interface (API), or also download it with its application (graphical user interface) for local usage (on the local computer or server).

Is Data FAIR (findable, accessible, interoperable and reusable): MESOCOSM was designed from the outset with maximum adherence to the FAIR principles that promote finding, accessing, interoperating, and reusing shared data (Wilkinson et al., 2016) by humans and machines. The proposed database system considers the principles of linked data mentioned in the works of Bizer et al. (Bizer et al., 2011; Pommier et al., 2019) demonstrating that each entity must be correctly identified with a persistent and unique identifier (PID),

[7] Ayadi, Ali, Jérôme Rose, Camille de Garidel-Thoron, Christine Hendren, Mark R. Wiesner, and Mélanie Auffan. MESOCOSM: A mesocosm database management system for environmental nanosafety. NanoImpact 21 (1 janvier 2021): 100288. https://doi.org/10.1016/j.impact.2020.100288.

described in a semantic format, and linked with other resources. The database content is registered and archived in different websites (the CEREGE website, GitHub repository and Perma web archiving service2) so that it can be easily found and accessible. Regardless of what may happen to the original source, the archived record will always be available through the cited websites. Similarly, all datasets have been published and are identified with unique DOI identifiers. MESOCOSM database have adopted a semantic format, the Resource Description Framework (RDF) which is used directly as the primary medium for linked data in MESOCOSM. All the entities in the database are linked to other resources with permanent unique URI identifiers through an ontology especially designed to support the development of the MESOCOSM database system for environmental nano-safety. These identifiers can be considered unique across the World Wide Web and therefore provide a solid basis for linking the MESOCOSM datasets. The adoption of the four FAIR characteristics, makes MESOCOSM a modern database making environmental exposure data valuable to a wide range of users, including manufacturers, researchers, and government agencies.

6. Deviations from the workplan

No deviations to be reported. The outputs of this task will be further expanded and updated over the course of the SAbyNA project.

7. Summary of work and recommendations for Task 2.2

7.1 Environmental exposure

In Task 2.1, a selection of tools and models have been assessed and distilled to those most relevant for SbD purposes. In general, the models are not suited to SbD requirements. Other issues include models not being accessible, lack of detailed documentation and a high level of expertise required to run models. GUIDEnano is the most promising and so the decision was made to select the most desirable features from models (e.g. algorithms, conceptualisations) and incorporate these into GUIDEnano. We have identified a number of areas for potential usability improvements in Task 2.2:

- Improving the accessibility of models where, models are developed within the consortium;
- Geographical consideration, including the creation of theoretical scenarios for SbD purposes;
- Model run times will be considered and the scope for improvements assessed when incorporating into GUIDEnano;
- Uncertainty and sensitivity analyses, including options for including environmental heterogeneity through uncertainty analysis, and using sensitivity analyses to determine the critical ranges of important parameters;
- Availability of input parameters, including scope for including default parameters

A number of methods and projects that generate methods have been assessed in Task 2.1. The field of method development for environmental exposure and release purposes is dynamic and work is ongoing currently to standardise nano-specific methods. We will keep abreast of these developments in Task 2.2, noting the projects that are actively working on this, and identify if there is the potential for method improvement based on this.

7.2 Human exposure

A number of tools and models have been distilled as part of Task 2.1. A key finding is none of the identified tools and models are individually suited for SbD requirements. Many of the tools and models also require intermediate to advanced risk assessment knowledge to operate, which may be an area of concern for SMEs. We have also identified that some of the tools and models are either not openly available or not updated regularly/at all, such as ANSES CB Tool and SUNDS. There is also an identified gap for dermal exposure models generally, where there are no nanospecific dermal tools and models associated to the transfer efficiency to skin. Risk of derm is available for bulk dermal exposure, whilst a dermal version of ART (dART) may soon be available. This gap will be reviewed for relevance as soon as it is available and updated as the WP develops.

For the tools and models, GUIDEnano will be used as the main tool with features from other tools/models used. This includes Precautionary Matrix for NMs, Control Banding Tool, ConsExpo Nano (relevant for consumer exposure and the paints case study), SUNDS and Stoffenmanger Nano. Potential usability improvements identified for further investigation in Task 2.2 include:

- Improving model assumptions including default values and other values used linked to exposure. This information may be limited;
- Improving the terminology used;
- Linking data to the models for default values. This is required for emission rates;
- Improving the input parameters. For example, it is unclear if a model/tool uses all the parameters and also how the model/tools reacts to small changes in a single parameter;
- Inter-user variability. We have established that there is inter-user variability in a number of the tools and models. This can also contribute to uncertainty;
- Improving algorithms within models (where this information is available);
- Uncertainty. This is one aspect that can be improved in the current tools and models. Three scenarios can be considered for uncertainty which are model uncertainty, parameter uncertainty and scenario uncertainty.

A number of methods have been distilled as part of this deliverable. These have been divided into two categories dustiness and release & exposure assessment and RMMs with the selection performed as listed in milestone 2.1. As part of the distillation process, data has been collected on which model input parameters the method uses, output variables and uncertainties. A variety of methods will need to be utilised for inputting the data required from selected models for input parameters.

A number of methods have been shortlisted for further investigation in Task 2.2. These are the five methods for dustiness (EN 17199-1, EN 17199-2, EN 17199-3, EN 17199-4 (also be investigated for experimental work) and EN 17199-5); ISO/DTS 21361:2019, CEN ISO/TS 21623:2018, EN 17058:2018, ISO/TR 18637:2016, ISO/TS 12901-1:2012, ISO/TS 12902-2:2012, ISO/TR 12885:2018, CEN ISO/TS 120252018 , ISO 28439:2011, EN 16966:2018 and ISO/TR 27628:2007 for release & exposure and RMMs methods. These methods are all nano-specific. Additional methods may also be distilled as required from the experimental work to be performed as the WP develops. Potential usability improvements identified for further investigation in Task 2.2 include:

- Method variables. A number of variables used by the method may be able to be changed and improved;
- Uncertainty of the method. Sources of uncertainty can include instrumentation, extrapolation of data and the quality of data used in an exposure assessment.

7.3 Data sources

Data Curation/Annotation/Standardisation:

In general the human exposure and environmental, fate and exposure work has lacked the advancements made compared to hazard data in terms of the use of ontologies, standardisation and harmonisation tools and developments. More recently, good progress has been made by the GRACIOUS and NanoFase projects with the development of standardised data collection templates and ontology for the release, fate and exposure data. A tool has been developed (GRACIOUS Wiki) to allow nano community provide input on the terms defined for the ontology to further harmonise the release, fate and exposure data curation. Suggestions will be provided in Task 2.2 for the use of standardised tools and data sources to make data standardised and annotated with meta-data.

Data Quality for modelling/risk assessment and SbD:

Data quality and data integrity is essential for any data to be useful for analysis and modelling. There has been some shortcomings in the quality of the data of some of the older projects due the way data was collected and not standardised. Good progress has been made by many ongoing nano projects (e.g. GRACIOUS, NanoInformatix etc.) to implement the data quality criteria for the data collection and scoring of the existing and newly collected data to inform about the data quality. Suggestions will be provided in the Task 2.2 for the implementation and use of quality criteria for the newly generated and existing datasets.

Data Accessibility:

Another critical issue is proprietary data and embargos of the datasets generated by the nano projects. Accessible means that data is always available and obtainable. Even if the data is restricted, the metadata should be open. Data should be made accessible by ensuring that it is retrievable online using standardised protocols and has restrictions in place if necessary. It is important to note that not all data has to be made open. Data needs to be as open as possible for allowing data exchange and reusability between researchers, institutions, organisations and countries.

FAIR Data:

FAIR principles provide guidance to scientific community for data management and stewardship of the data. These principles emphasise on machine action-ability (i.e. ability of computational systems to find, access, interoperate, and reuse data with none or minimal human intervention). We will provide general suggestions for making data FAIR and re-useable both by humans and machines.

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8. Annex 1 – Data Sources

8.1 List of data sources

Project Title	Website	Phys-chem	Toxicology	Ecotox	Exposure	Other	Database presence	Comments
GUIDEnano	www.guidenano.eu	Y		Y	Y		Certain	Exposure Scenario Data (Workers: 196, Service Life: 4); Web-based Risk Assessment Tool; ecotox data?
MARINA	http://www.marina-fp7.eu/	Y	Y	Y	Y		Certain	Phys-Chem 14 materials; In-vitro (8 cells types, 10 assay types, 209 Tests); In-vivo (8 Tests); Eco-tox data (40 Tests); Omics (Proteomics: 52 (substance x cell type x timepoint combinations), Metabolomics: 52 , Transcriptomics: 24); Exposure Scenario Data (Workers: 55, Service Life: 4); Most MARINA data transferred to e-NM instance (share w CALIBRATE & Nanoreg2);
NanoDefine	www.nanodefine.eu	Y					Unknown	Explores and develops conceptual and technical tools for the classification of materials. The NanoDefine e-tool, a decision support framework for the characterisation of potential nanomaterials.
NanoFase	http://nanofase.eu/	Y		Y	Y		Likely	Phys-Chem, EcoTox, exposure; Models; Poss data sharing? - DSA req;
NanoMICEX	http://www.nanomicex.eu	Y		Y	Y		Likely	Poss phys-chem, some ecotox & exposure data;
NanoMILE	http://www.nanomile.eu-vri.eu/	Y	Y	Y			Certain	MNM screening platform; ENM properties Knowledge Base; Phys-chem; in-vitro, in vivo; omics;
NanoPUZZLES	http://www.nanopuzzles.eu/	Y	Y				Certain	Modelling, analysis (QSAR & co); database & data standardisation info

NANoREG	http://www.nanoreg.eu/	Y	Y	Y	Y		Certain	NanoReg 1 data publicly avail in e-NM DB; phys chem, invitro & in vivo tox, ecotox, exposure; phys chem and tox templates
NanoReg2	http://www.nanoreg2.eu/	Y	Y	Y	Y		Certain	NanoReg 2 data accumulating in e-NM DB instance; phys chem, invitro & in vivo tox, ecotox, exposure;
GRACIOUS	https://www.h2020gracious.eu/							eNanoMapper DB established and data population ongoing;
NANOSOLUTIONS	www.nanosolutionsfp7.com	Y	Y	Y			Certain	Phys chem re 31 treated and untreated ENMs; Life cycle analysis; ENMs and BioMedia BioCorona; in-vitro cell models, with HTS; cross-species and environment ; disease and translocation studies; OMICs (mRNA, RNAseq; proteomics on beas2b, ecoli; closed proj,
SANOWORK	http://www.sanowork.eu	Y	Y		Y		Certain	Limited in-vitro results
SUN	http://www.sun-fp7.eu	Y	Y	Y	Y		Certain	Phys-Chem 8 materials; In-vitro (2 cells, 4 assay types, 17 Tests); In-vivo (9 Tests); Eco-tox data (205 Tests); Omics (Yes); Exposure Scenario Data (96 from NECID); Environment, Release Exposure (28 Datasets);
Nanomaterial Biological Interactions Knowledgebase	http://nbi.oregonstate.edu/	Y		Y			Certain	Knowledgebase (KB) on Nano-Bio interactions and NanoMaterial phys chem Library
Dana	http://www.nanoobjects.info/en/nanoinfo/knowledge-base	Y	Y	Y	Y		Certain	KB - Searchable for nano materials containing products
CaNanoLab - Cancer Nanotechnology Laboratory	https://cananolab.nci.nih.gov/caNanoLab/#/	Y					Certain	KB & Poss data source on materials in US database
Nanohub (US/NSF)	https://nanohub.org/	Y	Y				Certain (likely for phys-chem)	KB on risk assessment & standards etc; 320+ simulation tools/models ; some example nano DBs and datasets; nano education tools
MODERN	http://modern-fp7.biocenit.cat/index.html	Y	Y	Y			Certain	KB re emn QNPR modelling; database/data repository design; SbD
NanoMiner (FP7 NANOMMUNE project)	http://compbio.uta.fi/estools/nanommune/index.php/		Y				Certain	Optimised repository of OMICS data generated by NANOMMUNE project (see entry)

Nanoparticle Information Library	http://nanoparticlelibrary.net/	Y					Certain	KB by US NIOSH; Research database on emerging nanoparticles and their potential health effects
ITS-Nano (Intelligent Testing Strategy for ENMs)	https://www.safenano.org/research/its-nano/	Y	Y				Absent	KB re enm testing strategies; Ref - Stone V, Pozzi-Mucelli S, Tran L, Ashberger K, et al. 2014, "ITS-NANO - Prioritising nanosafety research to develop a stakeholder driven intelligent testing strategy," Particle and Fibre Toxicology, 11(9), 1-11.
ModNanoTox	http://www.birmingham.ac.uk/generic/modnanotox/index.aspx		Y				Likely	Re nano-tox modelling
OECD Database on Research into the Safety of Manufactured NMs	http://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm	Y	Y	Y	Y		Likely (Certain for ecotox)	Publications in the Series on the Safety of Manufactured Nanomaterials
NECID	http://www.perosh.eu/research-projects/perosh-projects/necid/				Y		Certain	NECID (Nano Exposure and Contextual Information Database) by PEROSH group Database system for detailed nano-exposure data and measurements; potential tool for use and as source of data from other projects
S2NANO	http://portal.s2nano.org/						Unknown	KB on modelling; links with OpenTox, NanoBank & NanoWiki
Serenade	http://www.labex-serenade.fr/labex-serenade						Unknown	KB and networking platform on ENMs Exposure and RA modelling
ENPRA	http://www.enpra.eu/	Y	Y		Y		Certain	Phys-Chem 12 materials; In-vitro (24 cells, 58 assay types, 650 Tests); In-vivo (17 Tests); IVIVE (83 Tests); Toxico-Kinetic Data (Yes) ; Exposure Modelling Data (Yes);
NANOMUNNE	http://www.safenano.org/research/nanommune/	Y	Y				Certain	Phys-Chem 50+ materials; In-vitro (8 cells, 12 assay types, 123 Tests);
CERASAFE	http://www.cerasafe.eu/						Unknown	KB on NM in relation to Ceramics production; Phys-chem characterisation, tox & Exposure tools development
eNanoMapper	https://enanomapper.net/	Y	Y	Y			Certain	Platform for EHS data repository; being adopted and used in Gracious and other projects (CALIBRATE, NanoReg 1 & 2, etc)
HSEnano	http://www.hsenano.com/en/						Unknown	KB on risk assessment & standards etc

NANOTEST	http://www.nanotest-fp7.eu/						Certain	Uploaded to NanoReg 2 (eNM); IOM in-vitro DB; poss sharing via DSA
CALIBRATE	http://www.nanocalibrate.eu	Y	Y		Y		Certain	Develop, integrate and validate models; sourcing data from other projects (eg MARINA); Modelling and Exposure information; continue to relate and poss data sharing agreements (DSAs)
PATROLS	https://www.patrols-h2020.eu/	Y	Y	Y			Certain	Started Jan 2018; ENM Phys-chem, in-vitro, in-vivo, ecotox; tox modelling; establish relations and poss DSAs
BIORIMA	https://www.biorima.eu/	Y	Y		Y		Certain	Started Noc 2017; ENM Phys-chem, in-vitro, in-vivo, ecotox; tox modelling; RMM toolbox establish relations and poss DSAs
ACENANO	http://www.acenano-project.eu/						Likely	Tools & data repository developments
IUCLID 6	https://iuclid6.echa.europa.eu/							Knowledge and Guidance on use & application of IUCLID 6 Standard/Format
NanoCommons	https://cordis.europa.eu/project/rcn/212586_en.html	Y	Y	Y	Y		Certain	Research and Innovation action to support networking & development: Joint Research Activities will integrate existing resources and organise efficient curation, preservation and facilitate access to data/models.
EC4SafeNano	http://www.ec4safenano.eu/						Unknown	EC4SafeNano aims to build an open collaborative network gathering expertise in risk management of nanotechnologies.
Hisents	https://hisents.eu/						Unknown	HISENTS aims to deliver an advanced nanosafety platform capable of providing high-throughput toxicity screening for the risk assessment of novel nanomaterials.
NanoGenTools	https://www3.ubu.es/nanogentools/						Unknown	NANOGENTOOLS combines toxicogenomics, proteomics, biophysics, molecular modelling, chemistry, bio/cheminformatics to develop fast in vitro high throughput (HTS) assays, with molecular based computational models for nanotoxicity.
NanoStreeM	http://www.nanostreem.eu/						Unknown	The goal of the NanoStreeM project is to promote good practices by identifying and implementing standards, identify gaps in methodologies and directions for further investigations in order to support governance of the occupational risk

								induced by the use of nanomaterials in semiconductor industry.
Pandora	https://www.pandora-h2020.eu/						Unknown	Project will compare the effects of a selected number of NP of wide application (iron, titanium and cerium oxide) on the immune response of several earth and marine organisms in parallel to human. The highly conserved system of innate immunity/stress response/inflammation will be the focus of PANDORA
SmartNanoTox	http://www.smartnanotox.eu/						Unknown	SMART TOOLS FOR GAUGING NANO HAZARDS
NICK	http://nikc.egr.duke.edu/#!/home						Certain	Largely literature data, but also NanoFASE project data being incorporated to via Nanocommons.
BIOMAX							Certain	Used to store data from NanoFASE project
NanoSolveIT knowledge base	Not publically available yet, though a publication is in progress. Sam has access (to some of the data, at least)						Likely	NanoSolveIT WP1 will create a knowledge base using NM "fingerprints" to enable read-across and grouping. Draws in pre-existing data and gap filling done with the project (WP2 experimental, WP3-5 modelling). Data will be stored in eNanoMapper.
TNO spatial release database	-						Likely	Spatial NM release database for all EU developed as part of NanoFASE project. Spatial database developed by TNO, using MFA outputs from EMPA.
Literature data								Data available in literature but not stored on any specific database.
LEITAT release data							Certain	Release data generated by LEITAT, e.g. TiO_2 road coating release rates. Most data will be held in different databases depending on the project (e.g. Biomax for NanoFASE, eNanoMapper for GRACIOUS).

NanoHarmony	https://nanoinfo.org/nanodatabank						Likely	NanoHarmony project, which has just started, aims to drive forward development of nano-specific guidance. Will include gap analysis and targeted experimental work. Includes tox (human and eco) and physchem characterisation.
NanoDataBank							Likely	UCLA database associated with MendNano and LearNano models.
Pubvinas	http://www.pubvinas.com/						Certain	A web-based nanomaterial database (developed in US) by big data curation and modelling friendly nanostructure annotations. Contains 705 unique nanomaterials covering 11 material types. Each nanomaterial has up to six physicochemical properties and/or bioactivities, resulting in more than ten endpoints in the database.
MESOCOSM	https://aliayadi.github.io/MESOCOSM-database/						Certain	The first centralized mesocosm database management system for environmental nanosafety containing experimental data collected from mesocosm experiments suited for understanding and quantifying both the environmental hazard and exposure.