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Development of a real-time information and monitoring system to support the risk assessment of engineered nanomaterials (ENMs) under REACH

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A2b. Report on detailed procedures to determine the validity of measured data

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Summary

The use of monitoring data under environmental monitoring programs requires a minimum of meta data and quality of measures that shall be implemented. Also for using existing monitored data under REACH, a minimum set of information data and quality criteria shall be considered and well explained in the Chemical Safety Report.

The aim of the present deliverable **DA2b "Report on detailed procedures to determine the validity of measured data"** is the description in detail of the requisites and criteria that should be considered in the determination of the validity of a measured data in order to be able to use them on the under relevant national and international monitoring programmes and REACH Regulation.

A complete description of the following criteria was provided within the deliverable D.A2.a. "Report on the information and quality criteria to use measured data under REACH and relevant monitoring programs":

- Appropriateness of the data for the specific process and occupational exposure scenario under investigation,
- Consideration of the role of risk management measures
- Availability of contextual information
- Information on the measurement and sampling methods and analytical techniques applied
- Number of data points
- Reproducibility and recovery
- Consideration of background concentrations of ENMs, including naturally occurring nanomaterials
- Spatial scale of the data (local vs regional)
- Description of the sources of exposure
- Information on the environmental behaviour and transformation of the ENMs

On the other hand, this task A2 aimed the characterization and description of the minimum meta-data needed to use measured data on the concentration of nanomaterials under relevant environmental monitoring programs, including specially air, water, soil, or sediments groundwater monitoring programs.

To this end, a complete evaluation of the information provided within relevant monitoring programs was conducted, including the definition of the specific criteria applied in each compartments, and included in the deliverable A2a. Key elements described within the task included:

- Recommended analytical methods
- Limit of quantification (LOQ)
- Recovery, accuracy and reproducibility of the data
- Time scale and date of sampling
- Recommended sampling protocols
- Source of pollution
- Contextual information (Temperature, humidity and pressure)

In the present deliverable A2b, a detailed analysis of the necessary considerations for the classification of measured data on the concentration of nanomaterials in the environmental, urban and industrial compartments was undertaken and detailed procedures for each compartments stablished.

A set of decision support procedures was developed, including procedures to define the validity of measured data to estimate the exposure to nanomaterials in the air, water, groundwater, sediment and soil compartments, as well as in industrial and urban environments.

Table of contents

1. Scope and goal of the deliverable

Task A2 of the NanoMonitor project deals with the "Definition of monitoring data information and quality requirements according REACH" and the main existing monitoring programs.

Deliverable DA2a "Report on the information and quality criteria to use measured data under REACH and relevant monitoring programs", focussed on the definition of the minimum data and data quality needed for using existing monitored data for exposure estimation in the exposure assessment of the Risk characterization process according REACH Regulation.

With that aim, after a brief introduction of the REACH Regulation and existing monitoring programs, the Risk Assessment process according REACH Regulation was explained in detail, mainly the Exposure Assessment step where the data on exposure estimation is needed. After that, the minimum information and quality criteria to use measured data under REACH was described.

Exposure estimations can be measured or modelled data. Different monitoring programs generating a data base of exposure estimations, including monitoring data for air pollution, water, wastes and soil exist. In the scope of the deliverable DA2a, minimum meta data accompanying measurements and the minimum quality control and assurance criteria for being useful, for exposure assessment under REACH and for the feeding of existing data bases, were also described.

In the present deliverable **DA2b "Report on detailed procedures to determine the validity of measured data"**, a detailed analysis of the necessary considerations for the classification of measured data on the concentration of nanomaterials in the environmental, urban and industrial compartments as valid without restriction, valid with restrictions or non-valid was undertaken and detailed procedures for each compartments stablished.

A set of decision support procedures were developed, including procedures to define the validity of measured data to estimate the exposure to nanomaterials in the air, water, groundwater, sediment and soil compartments, as well as in industrial and urban environments, in order to support the use of the excel tool for each compartment.

2. Introduction: monitoring data

2.1. Environmental monitoring programs

Monitoring data is composed of numerical data and associated information, often referred to as meta-data[1].**Fundamental metadata** required to support the monitoring data includes:

- the targeted chemical,
- analytical method and performance information for the analysis;
- sampling protocol;
- sampling location and time;
- information on the nature of the sample;
- other relevant information

Although some monitoring data are available, being collected for regulatory purposes or in the scope of different R&D&i projects, there exist several shortcomings for using them in exposure assessment and modelling purposes (application, calibration, validation), overall when dealing with chemicals substances at the nanoscale. The most **common critical deficiencies** related to the available current data are:

- Lack of information on the *context* in which the data were generated and clear objectives of the monitoring programme: representativeness (location, duration, frequency), address temporal variability of sources and system dynamics;
- The *quality of data* is not indicated and cannot be traced;
- Data presented are aggregated and *raw data* cannot be obtained;
- It is not clear whether the monitoring *data represent* hot spots or are representative of background conditions;

The identification of **the target chemical limit of detection and limit of quantification (defined by analytical method); sampling location and sampling time and frequency, are key elements** for using the data for exposure assessment confidently[¡Error! Marcador no definido.] . Thus, it is highly recommended that these meta-data elements are collected when comparing data compiled from different sources.

Quality assurance and quality control are important for high quality monitoring data. Key elements in guaranteeing the quality of monitoring data are: utilising reference materials; conducting inter-laboratory studies; and reporting the quality assurance procedures used in collecting the data.

When dealing with nanomaterials, it is important to mention that, up to date different problems make difficult the determination and overall quantification of nanomaterials when monitoring exposure levels in the environmental compartments and also at the workplace. These problems are related with:

- the lack of well stablished reference materials,
- Background of natural nanomaterials,
- No existing standardized protocols for the determination of the concentration at environmental, urban and industrial compartments,

[1] UNEP (2004).Guidance for a Global Monitoring Program on Persistent Organic Pollutants,1st Ed.,UNEP.

- No existing established standardized measurement units for all nanomaterials: at least mass concentration (units mg m^{-3}), but where possible also particle number (units m^{-3}) and/or surface area (units m^2 m^{-3}). The metric used to assess exposure to nanomaterials should be that which most closely links to any potential health effect,
- No existing sensible and specific analytical methods neither techniques which can probe nanomaterials speciation.

For risk assessment processes, **exposure level** determination is a key step. Release and exposure estimation under REACH aim to quantify the expected exposure when the conditions of use as described in the exposure scenario are implemented. Such quantification enables concluding on whether the risks can be adequately controlled. For each studied scenario, a corresponding exposure data set (for the various environmental compartments or various route of exposure to humans) is to be derived[2].

2.2. EC Regulation REACH

The REACH Regulation is the European Union's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC) No 1907/2006 [3] and its amendments until 1st of June, 2015. It represents a fundamental shift in the regulation of manufactured and imported chemicals in the European Union. Its main objective is to ensure a high level of protection of human health and the environment. REACH moves responsibility from authorities to industry to gather information on chemical substances and assess their safety. The provisions of REACH refer to substances (in whatever size or forms) and therefore also apply to nanomaterials, that are considered either as distinct substances or forms of a substance.

To ensure the safety, **REACH Regulation requires** to undertake a **risk assessment of chemicals**. Risk Assessment process is undertaken in three main steps which are:

1. Hazard assessment: identification and characterization.
2. Exposure assessment: definition of ES and exposure estimation.
3. Risk Characterization.

The first outcome of the exposure assessment is the generation of Exposure scenarios (ES) for the different uses. ES are sets of information describing the conditions under which the risks associated with the identified use(s) of a substance can be controlled. The conditions of use include:

- ✓ Operational Conditions (OC): duration and frequency of use, the substance amount used, or the process temperature
- ✓ Risk Management Measures (RMM): engineering controls, personal protective equipment, waste water treatment, exhaust gas treatment, etc.

[2] ECHA (2016). Guidance on Information Requirements and Chemical Safety Assessment. Part D: Framework for exposure assessment – Draft Version 2.0 (Public) April 2016.

[3] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006).

For each defined exposure scenario, expected exposure when the conditions of use as described in the exposure scenario are implemented is determined for risk characterization.

REACH Regulation requires that **existing adequately measured, representative exposure data** are taken into account in the exposure assessment, either **on their own or in combination with modelled exposure estimates**. Moreover, when dealing with nanomaterials, the use of simulation studies replicating the task or activity of concern should be taken into account when considering the use of measured data, especially considering the limitations of modelled estimates for nanomaterials. Risk assessor may then for example make use of monitoring data related to worker's exposure or releases to the environment from for example their own or of well-known customer site-specific information, and also from simulation studies and modelled estimates.

Considering that the **hierarchy for the use of exposure data when dealing with nanomaterials** would be preferentially[1] use measured data as first choice (having quantified key exposure determinants) and when not available, appropriate analogous data, including data derived from simulation studies. As the last option, modelled estimates would be used.

When dealing with occupational and environmental exposure assessment in the context of REACH, sources of measured data which could be used are:

- Measured data taken under the actual exposure settings for the exposure scenario to be developed (company data). For example, data generated to comply with other legislation or to evaluate the effectiveness of the RMMs in place. Measured data required for site licences and permits (with documented number/frequency of sampling, analytical methods, basic statistics) can be a good source of information for REACH.
- Exposure information from monitoring databases with regulatory purposes, when information requirements enabling a robust assessment are fulfilled.
- Exposure information from peer reviewed publications, when information requirements enabling a robust assessment are fulfilled.
- Biomonitoring data.
- Simulated process data.

In all cases, it is essential that used documentation is available and referred to in the Chemical Safety Report. In particular, a description of the methodology applied (for measurements/data collection) should be available as well as a reasoning why the data are considered relevant for the release estimation from the specific use/contributing scenario[4].

A critical point in the process is thus to clearly confirm that the employed **measured (or modelled) data** to be used for risk assessment purposes under the context of REACH is suitable for that purpose, regarding **quality criteria and information requirements**, which include precession, accuracy, correctness, representativeness, comparability and time coverage.

When measured datasets are used, there should be sufficient contextual information available to derive exposure scenarios (describing the conditions of use leading to exposure measured including any controls that are in operation)[2].

[4] ECHA (2016). Chapter R.16: Environmental exposure assessment. Version 3.0 – February 2016.

The purpose for which data were collected affects the further use of the data for REACH exposure assessment. It shall be taken into account when considering the **representativeness** of the data. Relevance of the of data source must be assessed. Issues to be assessed include:

- A basic condition for acceptance of the data set is that it should be **representative o**f the **operative conditions and risk management measures** described in the exposure scenario. Similarity and potential variations needs to be considered. A key requirement for the final outcome of an assessment is to be representative of the (contributing) scenario to be assessed. For instance, the RMMs prevailing during sampling (i.e. the generation of the measured data), should be similar (provide at least the same efficiency) as the ones reflected in the exposure scenario.

- In order for the data set to be applicable to a sector, it should represent the typical conditions within the sector suitable to assure safe use. Tasks that the data set represents should be clear.

The information needed **to** satisfactorily **support** the **suitability and representativeness** of the data, as **indicators of good quality**, are:

- ✓ reference to: quality schemes, standard sampling, and measurement methodologies;
- ✓ context: enough description to support the intended scope;
- ✓ clear description of monitored tasks;
- ✓ clear information on risk management measures in operation during sampling;
- ✓ details of duration and frequency of tasks and an assessment if the sampling duration is representative of full-shift exposure or only for the task duration;
- ✓ whether data are current rather than historical (i.e. sampling period to be reported);
- ✓ collection from a wide range of the sites and processes covered by the use description;
- ✓ statistical descriptors available.

Even in well-defined situations, available exposure data have substantial variability, and is strongly associated with implemented OC and RMM at the moment of measure. Both, **exposure variability** and representativeness (contextual, spatial, temporal) of the data to the settings to be assessed, need to be taken into account.

Measured data variability is reflected by the **spread of the distribution** of the individual exposure data points. This variability may be introduced through a number of factors, which include: differences in application of operational conditions, level of (substance) throughput, other local conditions, variability in performance of RMM, or behavioural differences between workers.

Exposure distributions can be reasonably described by the **geometric mean** (GM) and the **geometric standard deviation** (GSD). GM estimates the central tendency of the distribution, meanwhile GSD indicates the spread of the distribution.

On the other hand, **percentiles** show the percentage of the measured exposure levels that are at or below a certain value (e.g. the 90th percentile value indicates that 90% of the measured exposure levels are at or below that value). In general, the 90th percentile value of a distribution within a generally suitable dataset (i.e. a dataset corresponding to the conditions described in a contributing scenario) should be used as the exposure value for the risk characterisation. Under particular conditions, other percentiles may be applicable as well but a justification should be

provided. High values as well as values under the detection limit should remain in the distribution unless there is a sound justification from the assessor.

Finally, when it is not available appropriate representative measured data for the substance, an alternative is the use of measured data for analogous substances, if analogous substances have close enough physicochemical properties, or from analogous situations, a similar enough task, with justification, providing an appropriately conservative outcome.

A higher level of suitability, representativeness and quality of data shall be assured as higher is the concerns of hazard of the substance.

Therefore, present deliverable focuses on the definition of detailed procedures for establishing, in base on the defined minimum information and quality that shall be demanded to a data for being used in the Risk assessment of a nanomaterial, the validity of the data. Procedures classify a monitored data as valid without restrictions, valid with restrictions or no valid.

3. Particular considerations when dealing with environmental exposure data for nanomaterials

Apart from existing natural and accidentally produced nanomaterials, the production, use and disposal of engineered nanomaterials leads to the release of nanomaterials to the environment (industrial, urban and environment compartments) along their life-cycle. But nowadays, the exact amount of nanomaterials present in such compartments is not totally clear.

Measurement of the concentration of exposure to nanomaterials provides particular challenges. These include mainly the discrimination from background particles, collection and analysis of size information, effective high spatial and temporal variability, choice of metrics and measurement instruments, and measurement of high aspect ratio nanomaterials[5]. Other problems are related with:

- Hugh variety of existing nanomaterials (no grouping consensus)
- the lack of well stablished reference materials
- No existing complete standardized protocols for calculation of stream concentration
- No existing established standardized measurement units for all nanomaterials: at least mass concentration (units mg m^{-3}), but where possible also particle number (units m^{-3}) and/or surface area (units m^2 m^{-3}). The metric used to assess exposure to nanomaterials should be that which most closely links to any potential health effect.
- No existing sensible and specific analytical methods neither techniques which can probe nanomaterials speciation

The state of knowledge on these issues is continuing in developing and shall be taken into account when using measured exposure data.

Taking into account that limitations, different exposure data generating methods exists giving relevant environmental exposure data for nanomaterials. These methods can be divided into the three categories: **analytical methods *in situ*; simulation (pilot and laboratory scale studies) measurements and extrapolations; material mass flow analysis and simple models; probabilistic mass flow analysis; and kinetic modelling[6] [7].**

3.1. Analytical measuring methods for nanomaterials

Up to date, different analytical measuring techniques are available in order to provide data on the concentrations of nanomaterials in the environment. Techniques for measuring ultrafine particles and nanoparticles in air are most developed. Different works already investigates nanomaterials in water samples but still fewer work has been focused at nanomaterials concentration determination in sludge and soils.

[5] ECHA (2016). Guidance on Information Requirements and Chemical Safety Assessment. Part D: Framework for exposure assessment – Draft Version 2.0 (Public) April 2016.
[6] Milieu Ltd (2012). Final Report Environmental Exposure to Nanomaterials – Data Scoping Study. Service Contract No.07.0307/2011/610874/ETU/D.3
[7] ECHA (2012). Guidance on information requirements and chemical safety assessment. Appendix R14-4 Recommendations for nanomaterials applicable to Chapter R.14 Occupational exposure estimation

Analytical procedure includes the needed sample pre-treatment (digestion, extraction with solvent, etc.) to enhance sensitivity and selectivity. It is necessary to indicate this treatment when developing exposure assessment.

The analytical method determines applicable analyte species, sensitivity, selectivity and requirements for the pre-treatment of the sample. It also determines needed **sample pre-treatment** (digestion, extraction with solvent, etc.) to enhance sensitivity and selectivity. It is necessary to indicate this treatment when developing exposure assessment and different levels of sensitivity and selectivity could be noted when monitoring data are used in the exposure assessment.

3.1.1. Organic pollutants:

Analytical procedures for organic pollutants normally require some of the following pre-treatment of the sample: extraction, clean-up and concentration, before final instrumental analysis. Note from OCDE (2013): The clean-up step often determines the selectivity of the target chemical from the sample matrix and related isomers, but it is difficult to quantify the selectivity. Therefore, **method validation, interlaboratory comparison, round-robin studies and other QC procedures are especially important** to derive comparable data for exposure assessment purposes.

Examples of analytical methods for organic chemicals are presented in Table *1*:

Table 1. Examples of chromatographic analytical methods for organic chemicals.

Method	**Analyte**	**Sensitivity** (amount of signal response when changing concentration)	**Selectivity** (capacity of differentiate interferences of other substances)
Gas chromatography (GC)	Volatile to semi-volatile, mainly hydrophobic	Depending on the detector and analyte	Generally high, but depends on detector and analyte
Liquid chromatography (LC)	Hydrophilic compounds or non-volatiles	Medium to high	Generally, enough, but sometimes significant interference depending on detector and analyte
Gas Chromatography-mass spectrometry (GC-MS)	Volatile to semi-volatile, mainly hydrophobic	High	High
Liquid Chromatography-mass spectrometry (LC-MS)	Hydrophilic compounds or non-volatiles	Medium to high	High, especially when using detectors such as tandem MS (MS/MS) or time of flight (TOF) MS

3.1.2. Inorganic pollutants:

Examples of analytical methods for inorganic chemicals are indicated in Table 2. Pre-treatment normally requires digestion of the sample: different techniques of digestion exist and shall be indicated)

Table 2. Examples of analytical methods for inorganic chemicals

Method	Analyte	**Sensitivity** (amount of signal response when changing concentration)	**Selectivity** (capacity of differentiate interferences of other substances)
Atomic absorption	Major metal species	Low to high	High: sometimes spectrophotometric and matrix interferences
Inductively coupled plasma (ICP)1- atomic emission spectrometry (ICP-AES) or optical emission spectroscopy (ICP-OES)	Wide range of elements	Medium	High: sometimes spectrophotometric interference and/or matrix effects: wide dynamic range
Inductively coupled plasma - mass spectrometry2 (ICP-MS)	Wide range of elements	High	High: sometimes mass spectrometric Interference and/or matrix effects: wide dynamic range

3.2. Simulation studies

Different simulation studies at laboratory/pilot plant scale have been undertaken in order to study the fate and behaviour of nanomaterials in different scenarios, and thus aiming to validate the analytical procedures for nanomaterials determination in different matrixes[7].

3.3. Modelling of nanomaterials concentration

Regarding methods for modelling exposure to nanomaterials, probabilistic mass flow analysis treats the different parameters in the model as distributions. On the other hand, the computer simulations Monte Carlo and Markov Chain Monte Carlo are intended to generate estimates of sediment and groundwater concentration and also of emissions from production, manufacturing and recycling processes of nanomaterials and nanoproducts. Finally, kinetic models are those which specifically intends to reflect the dynamic behaviour and fate of nanomaterials in environmental compartments[6].

4. Required minimum information and quality of data to estimate exposure to nanomaterials

Data quality, referred as quality control and assurance, is determined by different activities and procedures:

- Use of reference materials
- Use of inter-laboratory studies (chemical-matrices)
- Reporting quality assurance in collecting data
- Possess certified laboratory or accredited analysis
- If no existing reference material or inter-laboratory studies, demonstrate by regular: blank analysis, spiked samples, duplicates and confirmatory analysis

The steps to follow are depicted in the decision tree schematized in Figure 1. In detail, each step corresponds with a decision relative to the metadata accompanying the dataset:

1. Classification, if not specifically stated, on whether the data come from **emission** (release of substances from a source into the environment) or **immission** (relates to the effects of emissions on the compartmental environments).
2. In case of air immission, it can be **environmental**, **urban / rural** or **occupational**, depending on the scenario in which takes place.
3. At the same time, if it is urban/rural or occupational, it can be produced in a closed space or **indoors**, or at the open air or **outdoors**.
4. Once the scenario is described, the origin of the dataset can be from a **model** or from case study **measurements**.
5. In each case, it is important that the **purpose and context** for which data were collected is clear and in line to support the intended scope; this affects how or if the data can be used in a REACH exposure assessment. Monitoring programmes may be designed to cover a large spatial area (high number of stations over a large territory), to achieve a high spatial resolution (high number of stations per area unit), or to monitor only one-point source release.
6. In the particular case of measured data, description of the measuring equipment is crucial to understand the purpose of the measurements as well as the analysis of the data carried out.

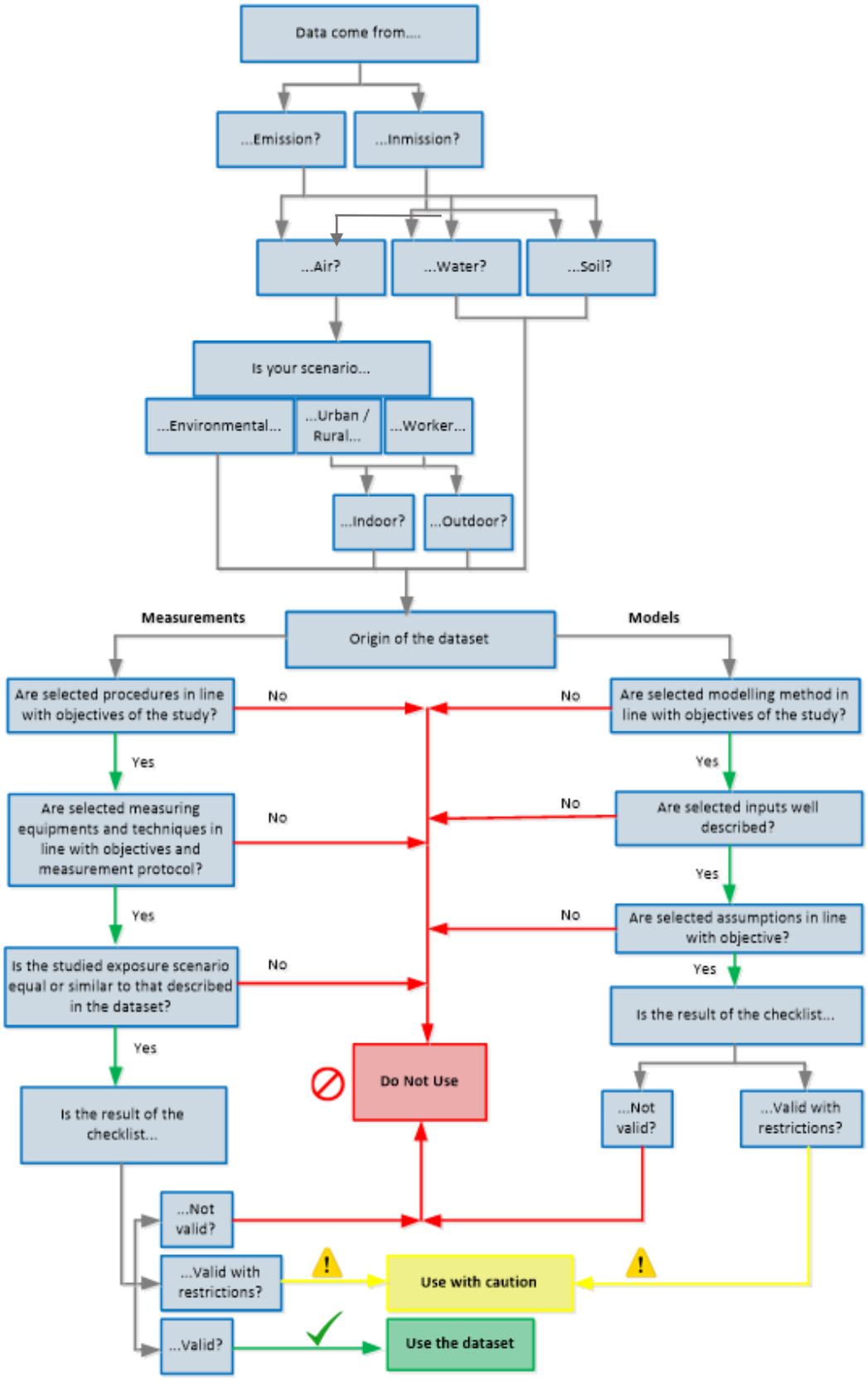

Figure 1. Decision tree to support the choice of the exposure assessment on the tool.

a. Thus, **specified sampling strategy** must be present in the context of the dataset, including what was sampled, when and where, how representative the samples were of the local or regional situation, and to what extent they allowed an assessment of temporal and/or spatial variability.
b. As well, the **analytical methodology** must be clearly described, either referring to a standard or internal protocol.
c. Finally, the **exposure scenario** on which was classified the dataset must correspond to the description given on the contextual information. That is, clear information on sites and processes covered by the measurements, details of duration and frequency of tasks and risk management measures present during sampling.

   If any of these criteria is not clear or absent, the dataset will not be reliable enough to be used with confidence.

7. In the case of simulated or modelled data, since in general several assumptions and quantitative information must be provided, it is fundamental that descriptors of the following are present:

   a. The **inputs** considered to be included on the model and how were they obtained, either from measurement data, simulations, bibliography, etc.
   b. The **assumptions** employed to include the inputs into the model must be explained and reasoned, since most of the information is quantitative, thus allowing a wide range of interpretation.

   If any of these criteria is not clear or absent, the dataset will not be reliable enough to be used with confidence.

8. In case of both paths have enough information to continue, it can be proceeded with the checklist from the tool, specifying the presence of actual meta-information of the data and fulfilling a score that will range the present metadata according to the importance within the REACH Regulation in one of the three categories, depending on the trustworthiness offered:

   - **NOT VALID**: Indicates that fundamental information is missing to ensure the completeness and reliability of the data set, and the data are weak or inconsistent to be used as part of a study.
   - **VALID WITH RESTRICTIONS**: Complementary information would be required to ensure the completeness of the data.
   - **VALID**: The data is reliable and complete and can be used with confidence within the REACH context to estimate the PEC or PNEL.

From Figure 1, it can be seen that due to the hierarchy of data sources within reach shown in section 2.2, only the status of “Valid with Restrictions” can be reached from modelled data, due to the quantitative nature of the assessment.

Bellow, a detailed required quality and minimum information for measured data is presented for each environmental compartment proposed in the scope of the NanoMonitor project. The aim of this decision support procedures is to define the validity of measured data to estimate the exposure to nanomaterials in the air, water, groundwater, sediment and soil compartments, as well as in industrial and urban environments, supporting the use of the excel tool for each compartment.

5. Procedures for data validity determination

5.1. Aim of the procedure

In the scope of the task A2 of the NanoMonitor project, a detailed procedure for data validity determination has been developed. It is a tool intended to be used by Risk assessors and stakeholders in order to decide the validity of an existing data for being used in the scope of the REACH Regulation.

5.2. Procedure of validation of an existing data

A set of decision support procedures were developed following the steps explained in section 4 of present deliverable, including procedures to define the validity of measured data to estimate the exposure to nanomaterials in the air, water & groundwater, sediment and soil compartments, as well as in industrial and urban environments, in order to support the use of the excel tool for each compartment. These **procedures aim to accompany the tool** with a process for data validity determination in order to explain in more detail fields which the tool is asking for.

Steps to follow up in the validation process are:

1. Determine type of data: air, water/groundwater or soil/sediment compartments, as well as in industrial or metropolitan environments.
2. Read details of required previous information and data quality on the corresponding procedure.
3. Determine the validity of the data using the corresponding checklist on the tool depending on **the exposure scenario.**

5.3. How the tool works

In a first step of the task A2 of the NanoMonitor project, the minimum required information and quality of data to be used in the scope of the REACH Regulation as well as in the main existing databases of monitoring programs was set and explained in detail. Such study is presented in the deliverable DA2a.

In a second stage, a **tool with a procedure for data reliability** determination has been developed. In that procedure, each of established data parameters (information and quality criteria) are contemplated as a checklist. The user can select in such checklist which parameters are available as metadata in the analysed dataset, obtaining an estimation of the consistency of such set of data. The set of 6 decision support procedures for each exposure scenario developed also in the scope of A2b are intended to guide user explaining in more detail fields which the tool ask for.

The starting sheet of the tool is shown in Figure 2 and shows a brief description of the aim of the tool and a step-by-step guidance on how to start using the tool. Firstly, the scenario most suitable to the data must be selected. This will guide to the corresponding sheet where a corresponding set of parameters is listed to be checked by the user of the data (see Figure 3 and Figure 4 for examples).

Figure 2. Starting sheet of the Reliability Assessment for Exposure Data tool.

The available scenarios are classified depending on their location (indoor/outdoor) and origin (occupational/urban/environmental/modelled). Table *3* describes each scenario in detail:

Table 3: Description of each Exposure Scenario classification along with examples.

Name	Description	Examples
Model	Data coming from a quantitative or qualitative theoretical modellization or software. Not measured. It will always have a higher degree of uncertainty, thus never reaching a 100% of reliability.	*REACHNano tool,ART tool, Stoffenmanager, self-developed tools….*
Worker Indoor	Data related with occupational exposure in a closed or inner environment.	*Factory, laboratory, pilot plant…*
Worker Outdoor	Data related with occupational exposure in an open air environment.	*Construction sites, quarries, open air mines…*

Urban Indoor	Environment in closed or inner areas of an urban area, independent of the size or population.	*Underground, schools, buildings, passages, home…*
Urban/Rural Outdoor	Open air in surroundings or within inhabited areas independently of their population.	*City streets, traffic lanes, villages, parks…*
Environmental emissions AIR	Refers to all the remaining scenarios of release of substances from a given source into the environmental compartment of air.	*Vulcans ash, marine aerosols, fires…*
Environmental emission-inmission WATER	Refers to all the scenarios of release or exposure of substances from a given source into the environmental compartment of water and groundwaters.	*Spills, waste water, rainwater, treatment plants…*
Environmental emission-inmission SOIL	Refers to all the scenarios of release or exposure of substances from a given source into the environmental compartment of sediment and soil.	*Spills, irrigations, mines…*

Each parameter is weighted according to the importance within the REACH Regulation, in such a way that some of them were stated as essential and their absence makes the studied exposure data directly considered as not reliable enough for their use or "NOT VALID". These are for example parameters related with the origin and references of the data, the aim of the study, the measuring protocol followed (in case there existed one), instrumentation employed for the measurements or analytical methodology to extract information from the raw data.

Depending on the cumulative weight of the selected parameters from each scenario, the tool will range the score achieved indicating if the studied data is valid without restrictions, valid with restrictions or not valid, depending on the type and precision of accompanied information supplementing the studied data. Each outcome will classify the data set indicating:

- **NOT VALID:** Indicates that fundamental information is missing to ensure the completeness and reliability of the data set, and the data are weak or inconsistent to be used as part of a study.
- **VALID WITH RESTRICTIONS:** Complementary information would be required to ensure the completeness of the data.
- **VALID:** The data is reliable and complete and can be used with confidence within the REACH context to estimate the PEC or PNEL.

The tool for data validation is developed in an Excel format as a procedure for data reliabiltiy, acompannies the present DA2b deliverable and will be available as well from the web of the NanoMonitor project.

5.3.1. Modelled data (any scenario)

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.

- **Data source**: author or affiliation, database of publication for reference on who provides the information.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.
- **Date of measurements** (xx/yy/mmm, month, year): allows temporal comparability and completeness.
- **Location of measurements** (GPS, province, country): essential for spatial comparability and completeness.
- **Exposure Scenario analysed:** To which industrial, occupational or environmental sector are the database referred.
- **Monitored task description:** Within the exposure scenario, description of the task carried out or the elements present in the scenario that could influence the results (i.e. RMMs, parallel tasks, etc.)
- **Model employed:** detailed explanation if other than an ECHA recognised method or an existing/already published method is used.
- **Input data information:** previous information considered to be included on the model and source (measurements, simulations, bibliography, etc.)
- **Assumptions:** explanation of the assumptions or standards considered to insert the inputs into the model.
- **Validation for nanomaterials:** whether the model considers distinct assumptions regarding special properties of the ENMs or not.
- **Attached schemes or pictures of the scenario:** useful for replicates and completeness of the information.

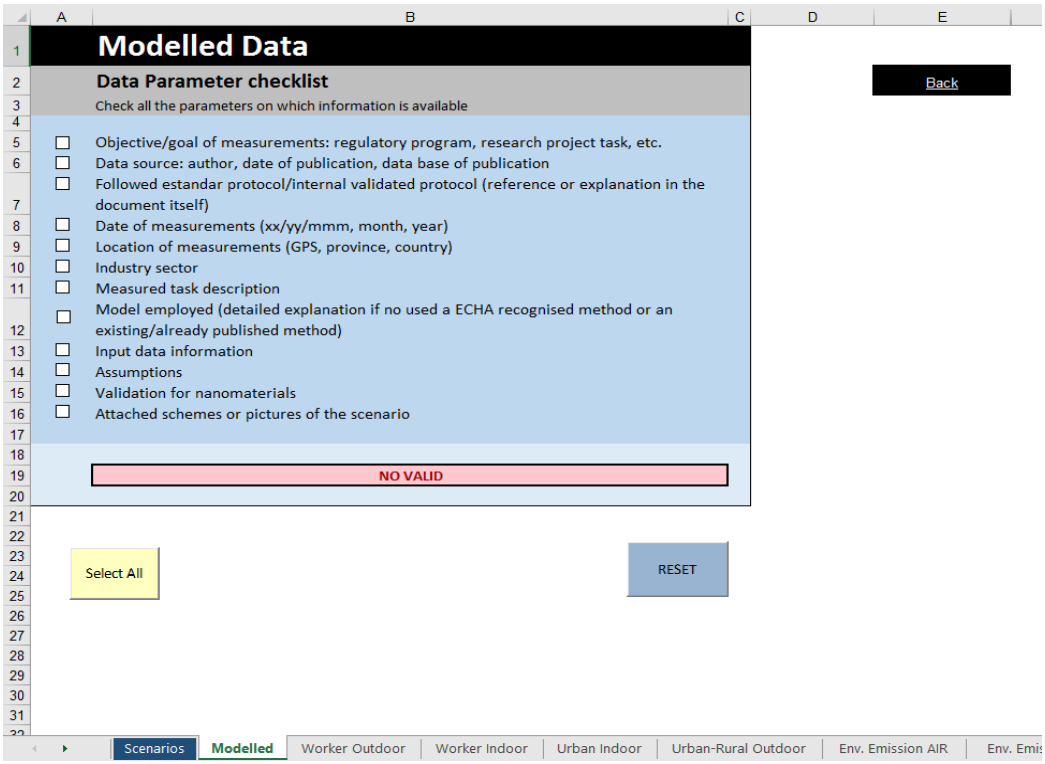

Figure 3. An example of one of the sheets of the tool describing a dataset coming from a model.

5.3.2. Human Exposure at Workplace

Properties are grouped in six different categories, Source information, Description of the scenario, Measurement data information, (Nano)Material information, Online measurement Information and Offline Measurement Information. Slightly differences discern the indoor and outdoor exposure (Figure *4*).

Indoor

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.
- **Data source**: author or affiliation, database of publication for reference and/or contact to the information provider.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.
- **Context:** Description of tasks and potential exposure routes. Detailed Operative Conditions and Risk Management Measures when sampling: the duration and frequency of the task and the measurements. Location of scenario (GPS, province, country); room volume; operating temperature and pressure conditions. Attached schemes or pictures of the scenario are useful as well for replicates and completeness of the information.
- **Date of measurements** (xx/yy/mmm, month, year): allows temporal comparability and completeness.
- **Exposure Scenario analysed:** To which industrial or occupational sector is the database referred.
- **Monitored task description:** Within the exposure scenario, description of the task carried out or the elements present in the scenario that could influence the results (i.e. RMMs, parallel tasks, etc.) and whether the task was intermittent, shot or continuous.
- **Substance description:** physicochemical properties: chemical composition, size and size distribution of the pristine material, matrix in which is embed, shape and chemical composition, fraction of nanomaterial on it and any other property that complete the information about the substance goal of the study.
- **Sampling strategy:** sampling points, sampling pattern, duration and frequency of sampling, flow rate, number of replicates, reference to the protocol if a standard followed, if Background and Near field/far field measurements present.
- **Analytical methodology for the data:** measured parameters and units (particle concentration, size distributions, mass distribution, surface area…), Integration period of the data (average of 10 min, 1 hour, 1 day, ...), average, uncertainty and statistical analysis of data, treatment of outliers and measurements under LOQ and any reference to protocol or standard used.
- **Measured fraction:** respirable, thoracic, inhalable.
- **On line analysis:** Description of the equipment employed and their capabilities: metrics, range, accuracy, sensitivity, resolution calibration and maintenance programs followed.
- **Off-line analysis (Filter-based air samples):** Characterise the size, shape and chemical composition of the released ENPs, equipment for sampling: personal pump, characteristics

of filter (material, diameter…), sample transport and conservation: recipient, conservation conditions, time until analysis, analytical technique employed (SEM, TEM, EDXS).

- **Reliability of the laboratory**: indicate if application of state-of-the-art GLP and QA/QC (ISO 17025), participation in international intercalibration and proficiency testing exercises; analysis of CRMs (certified reference materials) …

Outdoor

Apart from the previous information, some further indications are required when the measurements take place outdoors and that could influence the final exposure data:

- **Height of location and of the sampling placement of instruments**: respect to sea level, direction and strength of the flowrates to which the location is exposed.
- **Scenario area information:** Type of location (rural, urban, suburban) of the surroundings of the scenario, as well as proximity of other activities, secondary sources, type of influence: traffic, industry, background along with their intensity or distance to main focus.

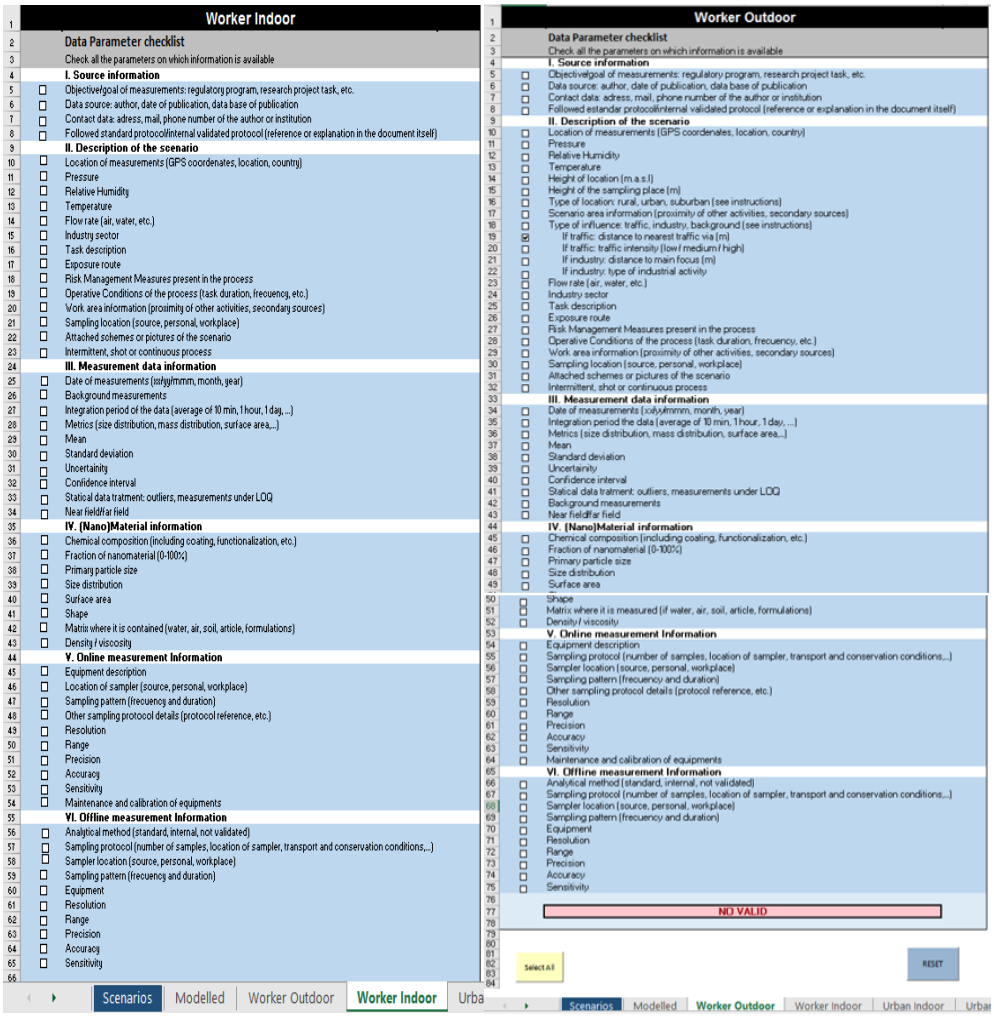

Figure 4. Another example of the developed NanoMonitor tool with a procedure for establishing the validity of an existing data of from occupational exposure to nanomaterials indoors (left) or outdoors (right).

5.3.3. Human Exposure at Urban/Rural settings

Properties are grouped in five categories, which are: source information, description of the scenario, measurement data information, online and offline measurement information. Slightly differences discern the indoor and outdoor exposures.

Indoor

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.
- **Data source**: author or affiliation, database of publication for reference and/or contact to the information provider.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.
- **Context:** Description of tasks and potential exposure routes. Detailed Operative Conditions and Risk Management Measures when sampling: the duration and frequency of the task and the measurements. Location of scenario (GPS, province, country); room volume; operating temperature and pressure conditions. Attached schemes or pictures of the scenario are useful as well for replicates and completeness of the information.
- **Date of measurements** (xx/yy/mmm, month, year): allows temporal comparability and completeness.
- **Exposure Scenario analysed:** Description to which industrial, urban or rural setting is the database referred.
- **Monitored task description:** Within the exposure scenario, description of the task carried out or the elements present in the scenario that could influence the results (i.e. RMMs, parallel tasks, etc.) and whether the process measured was intermittent, shot or continuous.
- **Substance description:** physicochemical properties: chemical composition, size and size distribution of the pristine material, matrix in which is embed, shape and chemical composition, fraction of nanomaterial on it and any other property that complete the information about the substance goal of the study.
- **Sampling strategy:** sampling points, sampling pattern, duration and frequency of sampling, flow rate, number of replicates, reference to the protocol if a standard followed, if Background and Near field/far field measurements present.
- **Analytical methodology for the data:** measured parameters and units (particle concentration, size distributions, mass distribution, surface area…), Integration period of the data (average of 10 min, 1 hour, 1 day, ...), average, uncertainty and statistical analysis of data, treatment of outliers and measurements under LOQ and any reference to protocol or standard used.
- **Measured fraction:** respirable, thoracic, inhalable.
- **On line analysis:** Description of the equipment employed and their capabilities: metrics, range, accuracy, sensitivity, resolution calibration and maintenance programs followed.
- **Off-line analysis (Filter-based air samples):** Characterise the size, shape and chemical composition of the released ENPs, equipment for sampling: personal pump, characteristics of filter (material, diameter…), sample transport and conservation: recipient, conservation conditions, time until analysis, analytical technique employed (SEM, TEM, EDXS).

- **Reliability of the laboratory**: indicate if application of state-of-the-art GLP and QA/QC (ISO 17025), participation in international intercalibration and proficiency testing exercises; analysis of CRMs (certified reference materials) …

Outdoor

Apart from the previous information, some further indications are required when the measurements take place outdoors and that could influence the final exposure data:

- **Height of location and of the sampling placement of instruments**: respect to sea level, direction and strength of the flowrates to which the location is exposed.
- **Scenario area information:** Type of location (rural, urban, suburban) of the surroundings of the scenario, as well as proximity of other activities, secondary sources, type of influence: traffic, industry, background along with their intensity or distance to main focus.

5.3.4 Environmental: Air

Some critical information about the environmental monitoring of immission or emission to the air of substances are listed in the following:

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.
- **Data source**: author or affiliation, database of publication for reference and/or contact to the information provider.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.
- The characteristics and **dynamics of the system**, detailed OC and RMM when sampling: the duration and frequency of tasks. Other close operations. Description of flow (Q, origin, destination, …)
- **Context:** Description of tasks and potential exposure routes. Detailed Operative Conditions and Risk Management Measures when sampling: the duration and frequency of the task and the measurements. Location of scenario (GPS, province, country); room volume; operating temperature and pressure conditions. Attached schemes or pictures of the scenario are useful as well for replicates and completeness of the information.
- **Date of measurements** (xx/yy/mmm, month, year): allows temporal comparability and completeness.
- **Exposure Scenario analysed:** Description to which industrial, urban or rural setting is the database referred.
- **Substance description:** physicochemical properties: chemical composition, size and size distribution of the pristine material, matrix in which is embed, shape and chemical composition, fraction of nanomaterial on it and any other property that complete the information about the substance goal of the study.

- **Sampling strategy:** sampling points, sampling pattern, duration and frequency of sampling, flow rate, number of replicates, reference to the protocol if a standard followed, if Background and Near field/far field measurements present.
- **Followed Standard[8] or internal validated method.**
- **Analytical methodology for the data:** measured parameters and units (particle concentration, size distributions, mass distribution, surface area…), Integration period of the data (average of 10 min, 1 hour, 1 day, ...), average, uncertainty and statistical analysis of data, treatment of outliers and measurements under LOQ and any reference to protocol or standard used.
- **On line analysis:** Description of the equipment employed and their capabilities: metrics, range, accuracy, sensitivity, resolution calibration and maintenance programs followed.
- **Off-line analysis (Filter-based air samples):** Characterise the size, shape and chemical composition of the released ENPs, equipment for sampling: personal pump, characteristics of filter (material, diameter…), sample transport and conservation: recipient, conservation conditions, time until analysis, analytical technique employed (SEM, TEM, EDXS).
- **Reliability of the laboratory**: indicate if application of state-of-the-art GLP and QA/QC (ISO 17025), participation in international intercalibration and proficiency testing exercises; analysis of CRMs (certified reference materials) …

5.3.5. Environmental: Water

Within the environmental monitoring techniques for immission or emission of substances into water, there are some general guidelines independently of the origin of the water body (rain water, sea, ground water, waste water, etc.). For the measurement of water parameters, different monitoring regimes are applied mainly differing in the sampling type. EN ISO 5667-1:2006 gives some guidance on sampling and distinguishes between continuous (on-line) measurement of specific parameters, periodic sampling, continuous sampling, composite sampling, and spot sampling.

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.
- **Data source**: author or affiliation, database of publication for reference and/or contact to the information provider.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.
- The characteristics and **dynamics of the system** (diffuse and point), detailed OC and RMM when sampling: the duration and frequency of tasks. Other close operations. Description of flow (Q, origin, destination, …)
- **Context:** Description of tasks, detailed OC and RMM when sampling: the duration and frequency of tasks. Description of flow (Q, origin, destination, …). Amount per industrial site [tonnes per day and year]; frequency of release from industrial site (e.g. if infrequent release only). Type of plant (standard municipal or site specific industrial with specific effectiveness); size of Biological Sewage Treatment Plant treatment plant; sludge treatment technique;

[8] JRC Reference Report on Monitoring (ROM) of emissions from IED-installations. RB/BS/EIPPCB/ROM_Final_Draft.
Access:http://eippcb.jrc.ec.europa.eu/reference/BREF/ROM_FD_102013_online.pdf

external treatment of waste. Flow rate of receiving surface water; place of use (indoor/outdoor). Attached schemes or pictures of the scenario are useful as well for replicates and completeness of the information.

- **Date of measurements** (xx/yy/mmm, month, year): allows temporal comparability and completeness.
- **Exposure Scenario analysed:** Description to which industrial, urban or rural setting is the database referred.
- **Substance description:** physicochemical properties: chemical composition, size and size distribution of the pristine material, matrix in which is embed, shape and chemical composition, fraction of nanomaterial on it and any other property that complete the information about the substance goal of the study. Concentration of substance in product; viscosity of liquid product; package design (or transport equipment) affecting release.
- **Sampling strategy:** sampling points, sampling pattern, duration and frequency of sampling, flow rate, number of replicates, reference to the protocol if a standard followed, if Background and Near field/far field measurements present.
- **Followed Standard[9] or internal validated method**
- **Analytical methodology for the data:** measured parameters and units Sample treatment: acidification, digestion, etc. Determination technique: Chromatography, Spectroscopy (FFF, ICP/MS, ICP/OES, FAAS), microscopy, gravimetric, etc. Selectivity, sensibility, accuracy, bias, repeatability, reproducibility, measurement interval, confidence interval (UNE-EN-3001), linearity, detection/quantification limit, uncertainty, robustness, validation (UNE-EN-ISO 8402). Statistical analysis: mean, outliers, LD/LQ (if LD>PNEC, reject). Sample transport and conservation conditions. Integration period of the data, average, uncertainty and statistical analysis of data, treatment of outliers and measurements under LOQ.
- **On line analysis:** Description of the equipment employed and their capabilities: metrics, range, accuracy, sensitivity, resolution calibration and maintenance programs followed.
- **Off-line analysis (Filter-based air samples):** Characterise the size, shape and chemical composition of the released ENPs, equipment for sampling: personal pump, characteristics of filter (material, diameter…), sample transport and conservation: recipient, conservation conditions, time until analysis, analytical technique employed (SEM, TEM, EDXS).
- **Reliability of the laboratory**: indicate if application of state-of-the-art GLP and QA/QC (ISO 17025), participation in international intercalibration and proficiency testing exercises; analysis of CRMs (certified reference materials) …

5.3.6. Environmental: Soil & Sediment

- **Objective/goal of the dataset**: any information referring to the monitoring or regulatory program, research project, university study, task, etc. to which the measurements form part of.
- **Data source**: author or affiliation, database of publication for reference and/or contact to the information provider.
- **Followed standard/internal validated protocol:** reference or explanation in the document itself on how the data was achieved, and for reproducibility of results.

[9] JRC Reference Report on Monitoring (ROM) of emissions from IED-installations. RB/BS/EIPPCB/ROM_Final_Draft.
Access:http://eippcb.jrc.ec.europa.eu/reference/BREF/ROM_FD_102013_online.pdf

- **Substance description:** physicochemical properties: chemical composition, size and size distribution of the pristine material, matrix in which is embed, shape and chemical composition, fraction of nanomaterial on it and any other property that complete the information about the substance goal of the study. Concentration of substance in product; viscosity of liquid product; package design (or transport equipment) affecting release.
- **Context**[10]: Description of conditions encountered at the site, including groundwater regime and surface water features. Plan showing monitoring and sample point locations. Description of site works and on-site observations. Details of response zone and other construction details of borehole monitoring installations. The characteristics and dynamics of the system
- **Relevant observations:** weather, soil horizons, DO, K, pH, Temperature, hardness, groundwater level (where groundwater monitoring is to be undertaken).
- **Sampling strategy:** the monitoring frequency, the monitoring locations, and media (soil and/or groundwater). Methods used for forming exploratory holes e.g. boreholes, trial pits, window samples. Rationale for sampling strategy e.g. if targeted rationale of targets; if non-targeted justification for spacing and layout. Frequency and timing of sampling. Locations, depths, area. Storage and transport conditions of samples.
- **Analytical methodology for the data treatment:** including adequately stringent limits of detection, measured parameters and metrics, Integration period of the measurements, average, uncertainty and statistical analysis of data, treatment of outliers and measurements under LOQ and any reference to protocol or standard used.
- **Followed Standard[11]or internal validated method.**
- **Reliability of the laboratory**: indicate if application of state-of-the-art GLP and QA/QC (ISO 17025), participation in international intercalibration and proficiency testing exercises; analysis of CRMs (certified reference materials).

[10] COMMUNICATION FROM THE COMMISSION European Commission Guidance concerning baseline reports under Article 22(2) of Directive 2010/75/EU on industrial emissions (2014/C 136/03). http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52014XC0506(01)&from=EN

[11] http://www.iso.org/iso/home/store/catalogue_ics/catalogue_ics_browse.htm?ICS1=13&ICS2=080&ICS3=05&

6. Conclusions

In the present deliverable **DA2b "Report on detailed procedures to determine the validity of measured data"**, and after the detailed analysis of the necessary information and quality requirements of data presented in deliverable A2a., considerations for the classification of measured data on the concentration of nanomaterials in the environmental, urban and industrial compartments as valid without restriction, valid with restrictions or non-valid was undertaken and detailed procedures for each compartments stablished.

A tool compiling these information and quality requirements accompanying to an existing data was created and presented in this deliverable. The tool is a procedure for data validity determination where user can select in such checklist which parameters are available. The procedure indicates if the studied data is valid without restrictions, valid with restrictions or no valid, depending on the type and amount of accompanied information and data quality of the studied data.

Moreover, a set of 6 decision support procedures was developed, including procedures to define the validity of measured data to estimate the exposure to nanomaterials in the air, water, groundwater, sediment and soil compartments, as well as in industrial and urban environments, in order to support the use of the excel tool for each compartment. They are intended to guide user explaining in more detail fields which the tool ask for.

7. Annex

Link to Excel Tool **"Reliability Assessment for Exposure Data.xlsm"**.

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