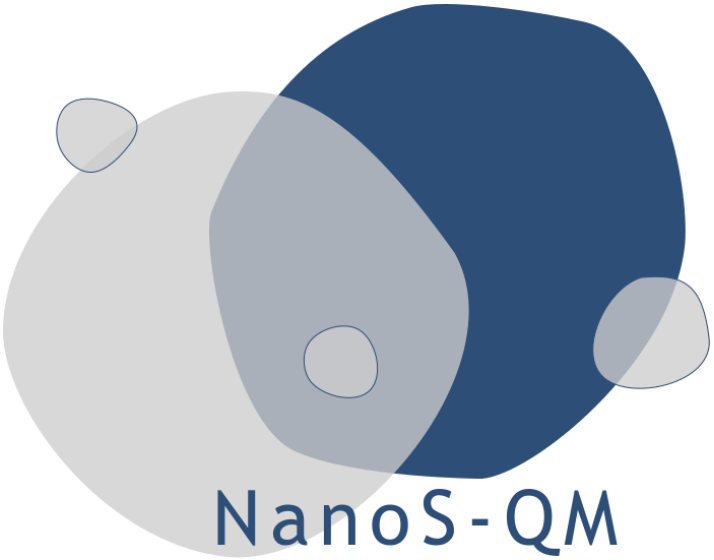
# Project NanoS-QM – Qualitäts- und Beschreibungsstandards für Forschungsdaten auf dem Gebiet der Nanosicherheitsforschung




NANOSAFETY IS USED AS AN EXAMPLE FOR TESTING QUALITY STANDARDS FOR MULTIDISCIPLINARY RESEARCH DATA

Nanoparticles are everywhere throughout everyday life and in the working environments – they make touchscreens conductive, increase the storage capacity of batteries, improve the compatibility of medicines and make components used in the construction sector lighter and more stable. Increased use in all areas of life means that more people are getting in contact with nanoparticles. The safe use of these materials therefore is significance for society beyond pure research. In the NanoS-QM project, the cooperation partners of the Leibniz Research Alliance Nanosafety are developing quality standards for data in this area. In doing so, they are creating the basis for improved and comprehensible risk assessment and regulation.

## General project information

Time frame: August 2019 – Juli 2021

Funding: Bundesministerium für Bildung und Forschung (BMBF)

Line of funding: Entwicklung und Erprobung von Kurationskriterien und Qualitätsstandards von Forschungsdaten

## Project partners

### Leibniz Institute for Information Infrastrukture

- Project leader
- Development of an interview guide
- Conducting the interviews with the project partners
- Evaluation and creation of a catalogue with quality criteria

### Leibniz Institute for New Materials

- Analysis of established characterization methods for the determination of toxicologically relevant nanomaterial properties
- Analysis of methods for the qualitative and quantitative determination of nanomaterials at the target site
- Determination of quality criteria for novel test systems (mechanical stress) for the respiratory tract
- Detection of test interferences
- Analysis of molecular key events

### Leibniz-Institut für Werkstofforientierte Technologien

- Evaluation of toxicologically relevant nanomaterial properties
- Characterization of nanomaterials
- Consistency assessment of data from different characterization methods

### Leibniz Research Centre for the Working Environment and Human Factors (IfADo)

- Development of an overview of alternative, complementary tests for the risk assessment of nanomaterials
- Sensitivity assessments based on the results for positive and negative controls
- Preparation of an overview of the use of homologous endpoints in the context of IVIVE
- Evaluation of the organ specificity of the in vitro systems used
- Research of existing regulations from OECD, ECHA, etc.
- Identification of data formats/metadata for subsequent use

### Leibniz Research Institute for Environmental Medicine

- Evaluation of detection methods for nanomaterials in tissues
- Recording of quality criteria of innovative toxicological 3D test systems for the respiratory tract and gastrointestinal tract
- Detection of test interferences
- Evaluation of the toxicological significance of readouts
- Collection of metadata from current in vivo and in vitro studies for the respiratory tract and GI tract
- Evaluation of metadata for in vitro extrapolation
- Deficit analysis based on interviews

## Results

### Experte workshop – Discussion on Existing Standards and Quality Criteria in Nanosafety Research

The partners of the research project NanoS-QM (Quality- and Description Standards for Nanosafety Research Data) identified and invited relevant experts from research institutions, federal agencies, and industry to evaluate the traceability of the results generated with the existing standards and quality criteria. During the discussion it emerged that numerous studies seem to be of insufficient quality for regulatory purposes or exhibit weaknesses with regard to data completeness. Deficiencies in study design could be avoided by more comprehensive use of appropriate standards, many of which already exist. The use of Electronic Laboratory Notebooks (ELNs) that allow for early collection of metadata and enrichment of datasets could be one solution to enable data re-use and simplify quality control. Generally, earlier provision and curation of data and metadata indicating their quality and completeness (e.g. guidelines, standards, standard operating procedures (SOPs) that were used) would improve their findability, accessibility, interoperability, and reusability (FAIR) in the nanosafety research field.

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### Description standards for multidisciplinary research data using the example of nanomaterials - Detailed table for data description facilitates subsequent use

The safety assessment of deliberately produced nanomaterials is a highly complex process to which scientists from various research fields contribute. Large amounts of data and descriptive metadata are generated which - provided they meet qualitative requirements and are described in detail - can be reused for the research and development of nanomaterials and nanoproducts as well as for predictions and risk assessment in a regulatory context. Possible health effects of newly developed nanomaterials could thus be identified more quickly, unnecessary repetition of experiments can be avoided, and the development of new, animal-free methods advanced. Researchers in the NanoS-QM project have determined which criteria interdisciplinary data and the associated metadata must meet in order to be used for the investigation of safety of nanomaterials.

*Aim of the study: Identifying suitable description standards and quality criteria for use in nanosafety assessment*

"Numerous standards and guidelines for the collection of data and metadata already exist. However, most of them are not specifically designed for nanosafety research and others are incomplete. For our study, we therefore selected existing guidelines and used them to create a catalog with descriptive information and quality criteria," explains Linda Elberskirch from the INM - Leibniz Institute for New Materials in Saarbrücken, lead author of the study.

The scheme created by the interdisciplinary team in the form of a table specifies which information must be recorded in an experiment to be able to (further) use the results for the assessment of nanosafety. As the table consists of several modules, researchers from all areas of nanosafety can use the scheme for aspects specific for their investigations. "For example, the scheme can be used by material scientists to describe the properties of a new material. This information is then called up by biologists who want to test the material on cell lines. They in turn also use the table, for example, to record detailed information on the

biological model used and the exposure to the nanomaterial under investigation in a standardized way," says Kunigunde Binder from FIZ Karlsruhe – Leibniz Institute for Information Infrastructure, describing the idea behind the project. The scheme was evaluated by experts during a workshop.

The table is divided into six overarching categories: general information, materials used, biological models, exposure, endpoints, and statistics and analysis. These categories are further subdivided into more detailed and specific subcategories. This makes the MIT Nanosafety more suitable for avoiding gaps in information transfer. To bring the table into use, the next step could be to add it to electronic laboratory notebooks (ELNs). "This would make the recording of all necessary data and metadata a daily routine and thus improve the reproducibility and reusability of experiments. Furthermore, this approach is particularly advantageous if we think about the rapidly increasing developments and applications of novel animal free test methods," adds Annette Kraegeloh, who was also involved in the study.

PUBLICATION: Linda Elberskirch, Kunigunde Binder, Norbert Riefler, Adriana Sofranko, Julia Liebing, Christian Bonatto Minella, Lutz Mädler, Matthias Razum, Christoph van Thriel, Klaus Unfried, Roel P. F. Schins & Annette Kraegeloh, Digital research data: from analysis of existing standards to a scientific foundation for a modular metadata schema in nanosafety. Part Fibre Toxicol 19, 1 (2022). https://doi.org/10.1186/s12989-021-00442-x

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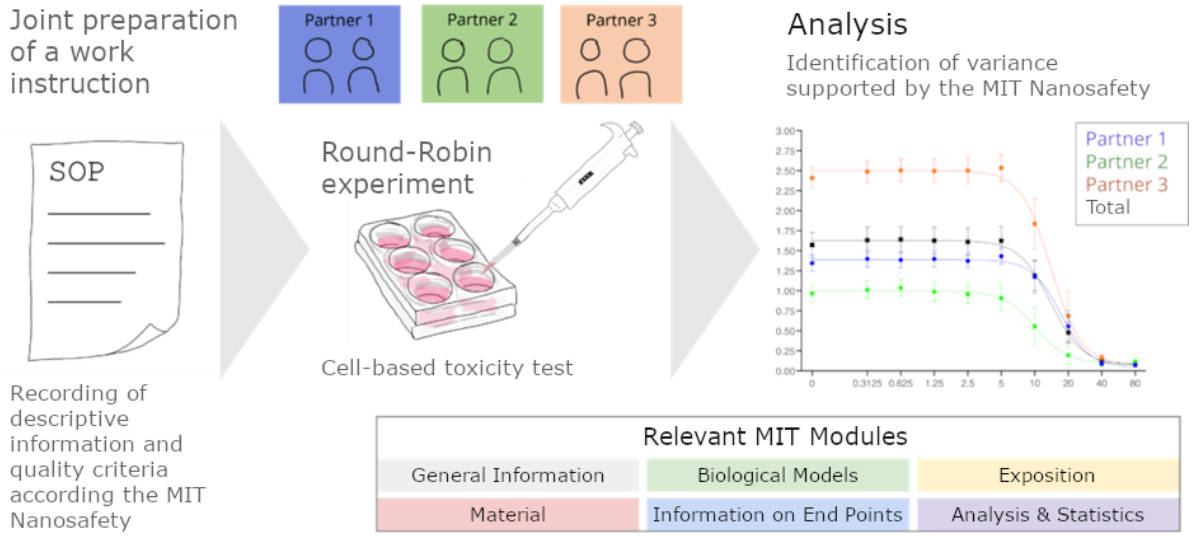
## How the structured collection of metadata makes studies on nanosafety more reproducible

Scientific studies on nanosafety are often not or not sufficiently reproducible. In addition, possible subsequent use is prevented by the fact that the results are difficult to find or incomplete. To prevent missing or misleading descriptions and data gaps in the future, the partners in the NanoS-QM project are proposing the use of the minimal information table - MIT for short - that they have developed. The MIT has now been tested in a round robin test at three institutes. Causes for differences in the final results obtained could be traced thanks to the MIT.

The safety of nanoparticles is assessed – even during the development process – using experiments in cell culture, which can supplement or in some cases even replace animal testing. "Modern test methods are very complex. If they are carried out by persons who, for example, have little experience in the method, undesirable sources of error can lead to results that are then misinterpreted. The purpose of the test also influences the test procedure and must be described. This is the only way we can know which results are relevant for which contexts and how the data can be used further," explains PD Dr. Christoph van Thriel from the Leibniz Research Centre for the Working Environment and Human Factors (IfADo).

In a recently published study as part of the NanoS-QM project, the researchers involved tested their solution approach, the minimum information table MIT, in a cell experiment designed as a round robin test: in three different laboratories at different locations, two experienced people performed the same frequently used test using a previously jointly prepared work instruction. Each of the six people repeated the test three times on different days. Each test point of the experiment was replicated four times. The procedures and any deviations from the work instructions were recorded precisely.




Dr. Linda Elberskirch, first author of the study from the INM - Leibniz Institute for New Materials in Saarbrücken, comments on the evaluation of the data: "We were able to calculate statistically exactly which parameters influenced the final results. The biggest differences were caused by the people carrying out the experiments. Thanks to the good documentation of the experiments, we were then able to trace the exact causes."

The MIT is therefore a good tool for creating work instructions and making experiments and their results more comprehensible. "Our approach is characterized by the fact that the data is recorded in a modular way. The approach can also be transferred to other branches of science. The future integration of the information retrieved at MIT into electronic lab notebooks can represent an important step towards the digital collection of structured data sets," adds PD Dr. Annette Kraegeloh.

Further development should focus on the availability of work instructions, metadata and research data and the linking of work instructions with the resulting data..

PUBLIKATION: Elberskirch L, Sofranko A, Liebing J, Riefler N, Binder K, Bonatto Minella C, Razum M, Unfried K, Schins RPF, Kraegeloh, A, van Thriel C, How Structured Metadata Acquisition Contributes to the Reproducibility of Nanosafety Studies: Evaluation by a Round-Robin Test. Nanomaterials 12:7 (2022) 1053. https://doi.org/10.3390/nano12071053

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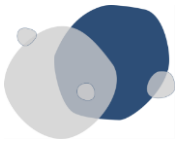
## Data standard for nanosafety research data published on 'FAIRsharing.org'

Partners of the Leibniz Research Alliance Advanced Materials Safety have published the results of one of their collaborations, a data guideline for description of research data called *Minimum Information Table for the Safety of Engineered Nanomaterials* (*MIT Nanosafety*), on the platform *FAIRsharing.org*. In addition, the guideline is also listed in the ELIXIR Toxicology Community Collection

The modular table resulted from the research project NanoS-QM (2019-2021, funded by BMBF). Collaborators of the preceding Leibniz Research Alliance Nanosafety (2012-2020) developed and tested quality standards for their research area. Their aim was to improve data quality in the complex and multidisciplinary research area of nanosafety for an improved and comprehensible risk assessment and regulation. Crucial was the collaboration of experts from different areas for development and thorough verification of all parts of the *MIT Nanosafety*.



Furthermore, the table was also assessed by external experts in a workshop and its usability was tested in a round robin experiment at different laboratories.

*FAIRsharing.org* is a platform, that describes and connects community-developed data and metadata standards, databases, repositories, and data strategies. The *MIT Nanosafety* is the only listed standard on *FAIRsharing.org* that maps the entire process of safety research for nanoparticles and that includes the most important scientific and regulatory standards. The modular approach allows scientists of all involved research areas of nanosafety to use the standard for the aspects they are examining.

Currently, the present partners of the multidisciplinary Leibniz Research Alliance Advanced Materials Safety are using the MIT Nanosafety for the development of functional and accepted, safe and sustainable advanced materials, especially also in the context of electronic laboratory notebooks.

TO THE ENTRY ON THE PLATFORM: https://fairsharing.org/5228

MORE INFORMATION INFOS: https://blog.fairsharing.org/?p=711