Data quality for Nanorisk Governance

Nanosafety Training School Venice, 21-25 June, 2021

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This project has received funding from The European Union's Horizon 2020 Research and Innovation Programme under Grant agreement 814530.

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- Data quality criteria
- Technology Readiness Level (TRL)
- **K**nowledge, Information **a**nd Data **R**eadiness **L**evel (KaRL)
- Conclusions (How KaRL could improve Nanorisk Governance)

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Data quality criteria

- Completeness
- Relevance (fitness-for-purpose)
- FAIRness (findability, accessibility, interoperability and re-usability)
- Traceability

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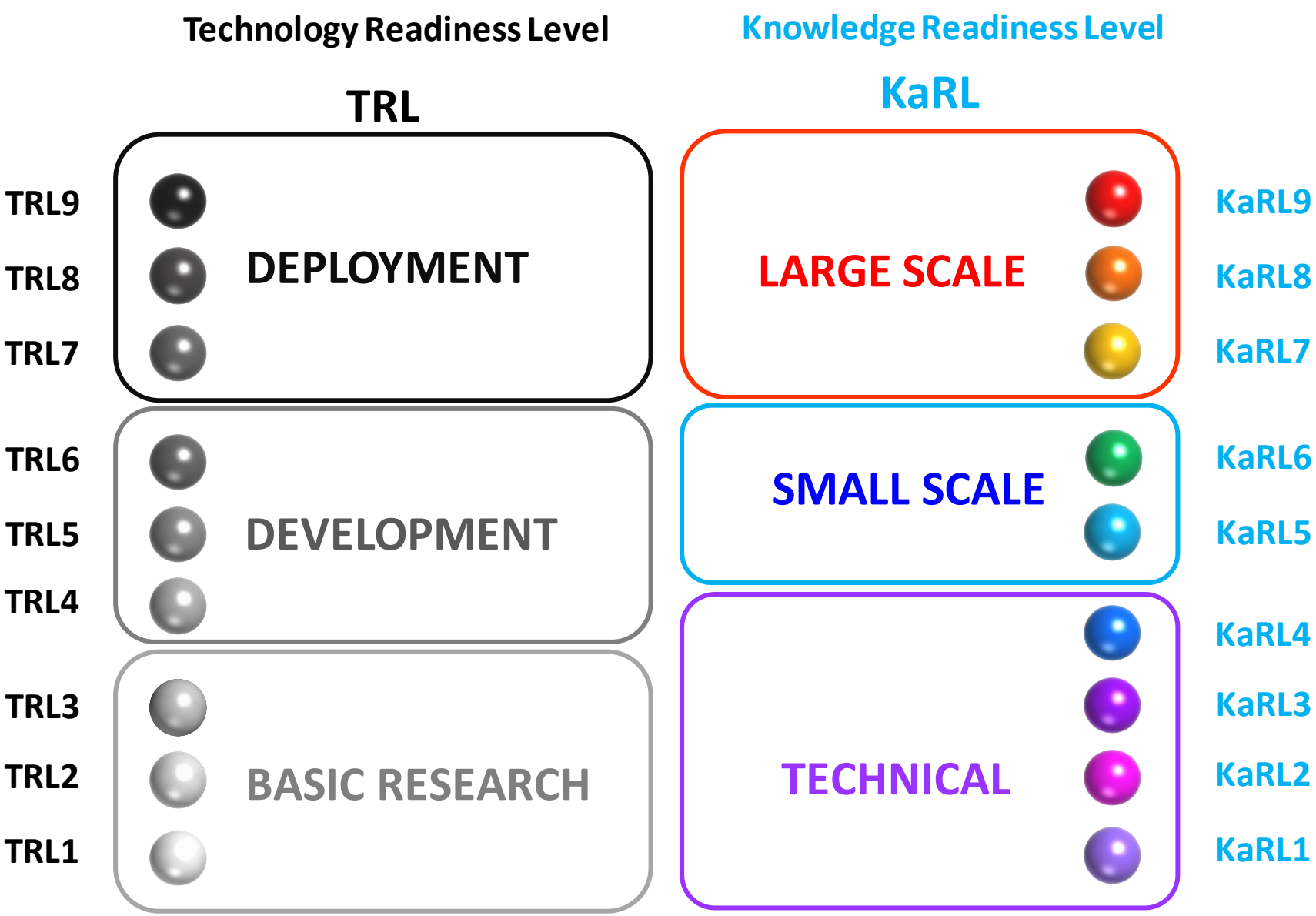
Analogy to Technology Readiness Levels (TRL)



KaRL1

ALL AVAILABLE DATA

digital

text files

ALL DATASOURCES

Physical libraries

Web of Science

Google Scholar

eNanoMapper

NanoCommons

CaLibrate

Lab books

EXAMPLE

Publications on nanomaterials (TiO2, ZnO, Au NP etc.)

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KaRL2

DATA COMPLETED WITH METADATA

Metadata

reference, structural,
statistical, bibliographic,
or technical metadata

Minimum reporting standards

ARRIVE	*in vivo* experiments using animals
MIAMETox	Microarray Experiment (modelling)
MIRIBEL	Protocols, exp. conditions
MINChar	Phys-chem. material characteristics
MIAN	Phys-chem. material characteristics

EXAMPLE

A study carried according to

MINChar

- *Particle size/size distribution*
- *Agglomeration state*
- *Shape….*

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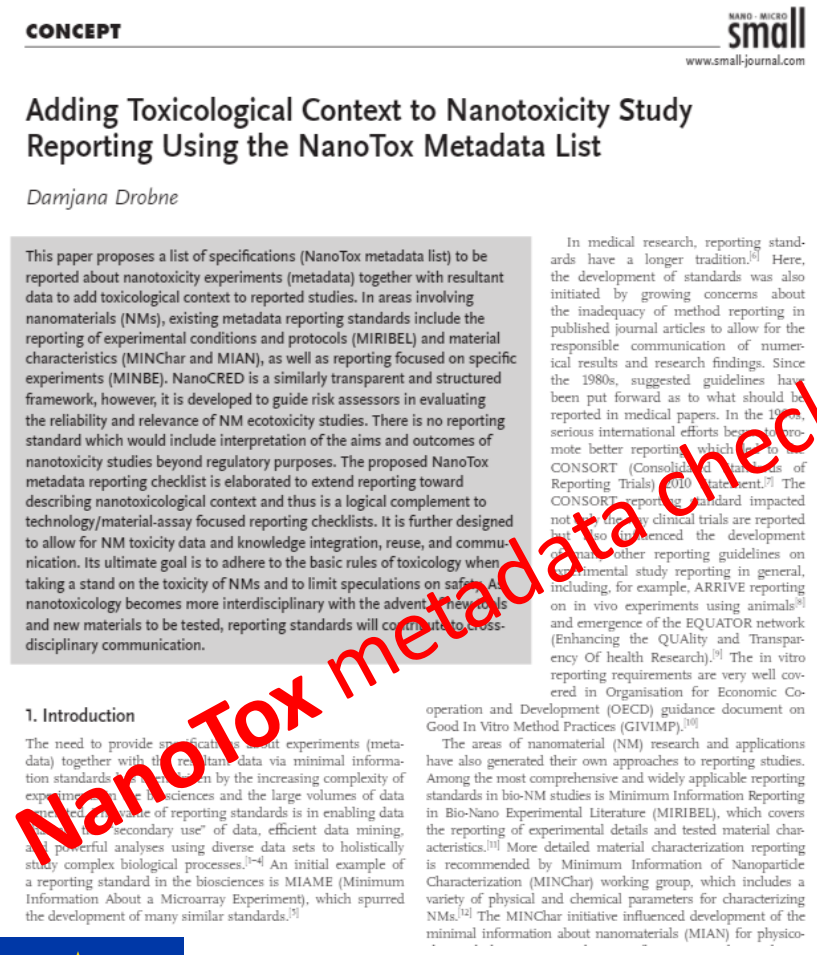
KaRL3

DATA COMPLETED WITH TOXICOLOGICAL CONTEXT



CONCEPT

small
www.small-journal.com

Adding Toxicological Context to Nanotoxicity Study Reporting Using the NanoTox Metadata List

Damjana Drobne

This paper proposes a list of specifications (NanoTox metadata list) to be reported about nanotoxicity experiments (metadata) together with resultant data to add toxicological context to reported studies. In areas involving nanomaterials (NMs), existing metadata reporting standards include the reporting of experimental conditions and protocols (MIRIBEL) and material characteristics (MINChar and MIAN), as well as reporting focused on specific experiments (MINBE). NanoCRED is a similarly transparent and structured framework, however, it is developed to guide risk assessors in evaluating the reliability and relevance of NM ecotoxicity studies. There is no reporting standard which would include interpretation of the aims and outcomes of nanotoxicity studies beyond regulatory purposes. The proposed NanoTox metadata reporting checklist is elaborated to extend reporting toward describing nanotoxicological context and thus is a logical complement to technology/material-assay focused reporting checklists. It is further designed to allow for NM toxicity data and knowledge integration, reuse, and communication. Its ultimate goal is to adhere to the basic rules of toxicology when taking a stand on the toxicity of NMs and to limit speculations on safety. As nanotoxicology becomes more interdisciplinary with the advent of new tools and new materials to be tested, reporting standards will contribute to cross-disciplinary communication.

1. Introduction

The need to provide specifications about experiments (metadata) together with the resultant data via minimal information standards is driven by the increasing complexity of experimental biosciences and the large volumes of data generated. The value of reporting standards is in enabling data "secondary use" of data, efficient data mining, and powerful analyses using diverse data sets to holistically study complex biological processes.[1–4] An initial example of a reporting standard in the biosciences is MIAME (Minimum Information About a Microarray Experiment), which spurred the development of many similar standards.[5]

In medical research, reporting standards have a longer tradition.[6] Here, the development of standards was also initiated by growing concerns about the inadequacy of method reporting in published journal articles to allow for the responsible communication of numerical results and research findings. Since the 1980s, suggested guidelines have been put forward as to what should be reported in medical papers. In the 1990s, serious international efforts began to promote better reporting, which led to the CONSORT (Consolidated Standards of Reporting Trials) 2010 statement.[7] The CONSORT reporting standard impacted not only the way clinical trials are reported but also influenced the development of many other reporting guidelines on experimental study reporting in general, including, for example, ARRIVE reporting on in vivo experiments using animals[8] and emergence of the EQUATOR network (Enhancing the QUAlity and Transparency Of health Research).[9] The in vitro reporting requirements are very well covered in Organisation for Economic Co-operation and Development (OECD) guidance document on Good In Vitro Method Practices (GIVIMP).[10]

The areas of nanomaterial (NM) research and applications have also generated their own approaches to reporting studies. Among the most comprehensive and widely applicable reporting standards in bio-NM studies is Minimum Information Reporting in Bio-Nano Experimental Literature (MIRIBEL), which covers the reporting of experimental details and tested material characteristics.[11] More detailed material characterization reporting is recommended by Minimum Information of Nanoparticle Characterization (MINChar) working group, which includes a variety of physical and chemical parameters for characterizing NMs.[12] The MINChar initiative influenced development of the minimal information about nanomaterials (MIAN) for physico-

NanoTox metadata checklist

Study (assay) aim
Toxicity/safety study
Mode of action study
Substance prioritization approach
Substance persistence/body burden study
Compliance with **ARRIVE** guidelines
Material description by using other reporting standards
MINChar or MIAN
MIRIBEL
nanoCRED
Minimum reporting details on study design
Acute exposure (single dose/exposure)
Chronic exposure
Multiple dose/exposure
Route of administration/exposure
Body distribution
In vitro (use ARRIVE reporting)
Positive control (material, substance)
Positive control (endpoint)
Compliance with MIRIBEL guidelines
Compliance with nanoCRED guidelines
Type of toxicity data (values) produced
Toxicity data /values: NO(A)EC(L), LO(A)EC, EC
Benchmark dose (BMD)
Benchmark concentration (BMC)
Reference dose (RfD)
Reference concentration (RfC)
Body burden data
Data on biokinetics
Data on toxicokinetics
ACDE
ADME
Endpoints measured/Endpoint selection principles
Target endpoints
Nontarget endpoints
Critical (key) endpoints
Secondary/comparative endpoints
Integrated endpoints
Hazard identification
Decision points on hazard/safety
Data on hazard

EXAMPLE

Toxicity, Hazard, Safety, Exposure

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KaRL4

FITNESS-FOR-PURPOSE

Evaluation of a dataset or a study on **fitness-for purpose**

Purposes: scientific, regulatory, safe-by-design, exposure assessment

Quality scoring systems

nanoCred

GuideNano

Klimish Scoring

DaNa

EXAMPLE

A study fit for regulatory purposes according to Klimish Scoring system

Score	Description
1	Reliable without restriction
2	Reliable with restriction
3	Not reliable
4	Not assignable

DaNa's Literature Criteria Checklist for toxicological publications

- *Physcochemical properties*
- *Sample preparation*
- *Testing parameters*
- *SOPs, OECD guidelines*

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KaRL5

List of stakeholder-specific requirements

Stakeholder-specific additional requirements to solve a task (e.g. answer a risk-related question)

EXAMPLE

Task/Need/Question: *Is exposure to particles in the working environment affecting the worker's lungs?*

Stakeholder-specific requirements:

- Occupational exposure to NPs (Legal requirements for these NPs)
- *in vivo* data on the effects of NPs on lungs
- COmbined Dosimetry (CoDo) or other tools or models for additional information
- New experiments if necessary

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What is an actionable document

An "**actionable document**" is a written instrument or **document** on which an **action** or defense is founded.

Metanalysis

Proposals

Explanations

Reports

Scoping review

Dossier

Opinions

Comments

Values

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KaRL6

FUNCTIONAL KNOWLEDGE in a from of **ACTIONABLE DOCUMENT**

EXAMPLE

Report on toxicity of **NPs** for an **industrial producer**

Actionable documents

Proposals
Reports
Dossier
Opinions
Comments
Explanations

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KaRL7

ACTIONABLE DOCUMENT quality-checked

A specialized governance authority is suggested to perform quality check of the actionable document

Governance authority

EXAMPLE

A DOSSIER on a NM for an authority

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KaRL8

Requirements for Large scale (risk governace)

BROAD CONTEXT

Needs of ALL stakeholders

Public Academia Industry Regulator

EXAMPLE

List of requirements

Public opinion

SEIN principles

Circular Economy principles

Safe-by-Design principles

Good governance principles

Impact assessment

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KaRL9

ACTIONABLE DOCUMENT READY for RISK GOVERNANCE

A document including KaRL1-7 and the requirements from KaRL8

Such document represents the basis for regulatory decisions

EXAMPLE

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **Titanium dioxide**

EC Number: **236-675-5**

CAS Number: **13463-67-7**

The proposal was submitted by **France** and received by RAC on **27 May 2016.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

France has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **31 May 2016**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **15 July 2016**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Normunds Kadikis**

Co-Rapporteur, appointed by RAC: **Norbert Rupprich**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **14 September 2017** by **consensus**.

+

Public opinion

SEIN principles

Circular Economy principles

Safe-by-Design principles

Good governance principles

Impact assessment

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NANORIGO

LARGE SCALE

KaRL9	**FUNCTIONAL KNOWLEDGE** for **RISK GOVERNANCE**
KaRL8	**Requiremets** for **RISK GOVERNANCE**
KaRL7	**Quality check** of **FUNCTIONAL KNOWLEDGE**

SMALL SCALE

KaRL6	**FUNCTIONAL KNOWLEDGE**
KaRL5	**SH-specific requirements**

TECHNICAL READINESS

KaRL4	**FITNESS-FOR-PURPOSE**
KaRL3	**+ SEMANTIC METADATA**
KaRL2	**+ METADATA**
KaRL1	**ALL AVAILABLE DATA**

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KaRL Assignment

Requirements	KaRL 1	KaRL 2	KaRL 3	KaRL 4	KaRL 5	KaRL 6	KaRL 7	KaRL 8	KaRL 9
Data exist	✓	✓	✓	✓	✓	✓	✓	✓	✓
Accessibility		✓	✓	✓	✓	✓	✓	✓	✓
Metadata completeness (MINChar, MIAMETox)		✓	✓	✓	✓	✓	✓	✓	✓
Semantic metadata with toxicological context (NanoTox met.checkl.)			✓	✓	✓	✓	✓	✓	✓
OECD guidelines				✓	✓	✓	✓	✓	✓
SOPs				✓	✓	✓	✓	✓	✓
Fitness-for-Purpose criteria (Klimish, DaNa, NanoCred, GuideNano)				✓	✓	✓	✓	✓	✓
Legal requirements					✓	✓	✓	✓	✓
Can question be answered					✓	✓	✓	✓	✓
Is it an actionable document						✓	✓	✓	✓
Is an actionable document quality checked: fullfills requirements							✓	✓	✓
Actionable document is traceable							✓	✓	✓
Requiremets for broad context								✓	✓
SEIN								✓	✓
Circular Economy								✓	✓
Safer-by-Design								✓	✓
Good governance principles								✓	✓
Does an actionable document contain KaRL1-8									✓

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How KaRL could improve Nanorisk Governance

- KaRL could support any stakeholder in providing a guidance on how and where to get high-quality data (**KaRL1-4**)
- KaRL helps to obtain reliable knowledge from data and a higher knowledge readiness for different purposes (**KaRL5-6**)
- Provides list of useful nanoinformatical tools to fill knowledge gaps
- Suggests quality check of actionable document by a specialized trusted governance authority (**KaRL7**)
- KaRL enables involvemnt of all stakeholders and addresses ethical, social issues (SEIN), Safe-by-Design, Circular Economy and Sustainability (**KaRL8-9**)

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Acknowledgements

- We greatefully acknowledge the **The European Union's Horizon 2020** for the financial support of the project NANORIGO (**Grant agreement 814530**)

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Thank you for your attention!

Are there any questions?

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