

NANoREG

Grant Agreement Number 310584

Deliverable D 1.12

Toolbox

(DoW version Approved by EC 25 May 2016)

Due date of deliverable: 2017/02/28

Actual submission date: 2016/12/11

Author(s) and company:	JRC
Work package/task:	WP1/ Task 1.07
Document status:	draft / <u>final</u>
Confidentiality:	confidential / restricted / <u>public</u>
Key words:	

DOCUMENT HISTORY

Version	Date	Reason of change
1	2016/12/11	Final draft submitted to NANoREG MC for approval
2	2017/02/16	Final version for upload to CIRCABC and EC participant portal
3	2017/03/24	Project Office harmonized lay-out

This work is licensed under the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.

To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-sa/4.0/> or send a letter to Creative Commons, PO Box 1866, Mountain View, CA 94042, USA.

*This project has received funding from the European Union
Seventh Framework Programme (FP7/2007-2013)
under grant agreement no 310584*



Lead beneficiary for this deliverable: Joint Research Centre, JRC, 02

Owner(s) of this document	
Owner of the content	JRC, 02
Co-Owner 1	
Co-Owner 2	
Co-Owner 3	
.....	

Table of Content

1	DESCRIPTION OF TASK 1.7	4
2	DESCRIPTION OF WORK & MAIN ACHIEVEMENTS	4
2.1	SUMMARY	4
2.2	BACKGROUND OF THE TASK	5
2.2.1	Identification of the concept of 'Tool' in NANoREG	5
2.2.2	Scope and organisation of the NANoREG Toolbox	5
2.2.3	How tools are reported	6
2.2.4	Proposed 'types' of tools	7
2.2.5	Estimated regulatory status of a tool	7
2.3	RESULTS	8
2.4	EVALUATION AND CONCLUSIONS	9
2.5	DATA MANAGEMENT	9
3	DEVIATIONS FROM THE WORK PLAN	9
4	REFERENCES / SELECTED SOURCES OF INFORMATION	9
	ANNEXES	9

1 Description of task 1.7

(From the DoW)

Task 1.7 NANoREG Instruments Toolbox for regulators and legislators

Implementation of the framework developed in task 1.4 needs that all tools recommended by Task 1.3 (following from the results of the WPs 2-6) and 1.2, as well as the recommendations from Task 1.6, be prepared and consolidated for the regulatory authorities and other users as part of a "NANoREG Toolbox". The NANoREG Tool Box, which ideally could be integrated or connected with the data platform and linked with relevant related toolboxes, will provide the regulators and legislators, as well as other stakeholders, with decision-supporting instruments for the short to medium term. This tool box will assemble in a structured way the instruments developed particularly by WP 3 and WP 6 in the form of guidance documents and/or decision-making tools and should be organised in such a way to enable regulators and other users to identify and use the most appropriate tool(s) to address their particular question(s) in nanomaterials safety management. WP 1 Partners will take leadership on the aspects in which they are involved in WP 5 and 6. It is also foreseen that ENEA develops a NMs-specific LCA guidance document in compliance with the ILCD Handbook, as well as an online tool for elaborating NMs exposure scenarios.

(Lead: JRC contributors: FOPH, RIVM, AIT, BfR, NRCWE, TCD, CEA, ISS, INERIS, IOM, NILU, VN-Ecamricert)

2 Description of work & main achievements

2.1 Summary

The NANoREG Toolbox is the second major project output after the Framework (D1.11). It supports the implementation of the Framework by providing an overview of test methods, datasets, models, guidance documents, decision trees, etc., useful to regulators and other stakeholders in the European REACH legislative context. The tools are generally arranged based on their link(s) to each section of the Framework document (see 2.2.2 below).

The sources of the 'tools' are, at first, the scientific deliverables of NANoREG. These contain test methods, SOPs, proposed decision trees, etc. Secondly, many other initiatives, at European level and beyond, have been scanned looking for useful tools that address one or more 'nano-specific hurdles' in safety assessment, as identified in the NANoREG Framework (D1.11).

The Toolbox presents an attempt at organising the information according to 'type' of tool and to 'regulatory maturity' of the tools. It also makes a distinction between actual (presently available and tested) tools and prospective (promised) ones. For a full discussion of these concepts, please refer to sections 2.3 and 2.4 below.

The resulting two large Excel[®] worksheets offer a rather complete and wide review of categorised tools, with descriptive information and metadata attached to them (in the worksheet rows). As such, D1.12 is a precious dataset of tools, available to the global nanoEHS¹ community, be it regulators or industry, ready for further expansion and exploitation. Making the use of the dataset user-friendlier than via an Excel[®]-based system was unfortunately not within reach of task 1.7 or JRC, due to limited resources available. As suggestion for the future users and further developers of the Toolbox, it should be rather simple to turn this Excel[®]-based dataset into a Wiki-like set of webpages for easy access and browsing.

Just like the Framework, this large Toolbox is released in NANoREG to become eventually publicly available at the end of the project (end February 2017). The Excel[®] files will be linked to a unique literature identifier in early March 2017, so that they can be easily referenced to by those who wish to exploit them under CC BY-NC-SA² licence, as foreseen by a recent NANoREG Consortium Agreement update. This Toolbox is also a building block for the White Paper of the EU-funded Horizon 2020 project ProSafe.

¹ Nanomaterials environment, health and safety.

² Creative Commons BY-NC-SA 4.0 International License <https://creativecommons.org/licenses/by-nc-sa/4.0/>

2.2 Background of the task

In order to make the Framework developed in task 1.4 (D1.11) a useful and workable NANoREG output, for all the nano-specific issues it highlights and (novel) strategies it presents, there should be one or more 'tool' available to regulators / industry, so that the safety assessment case at hand can be tested using them. As planned in the NANoREG DoW, all tools recommended by the deliverables (the results) of the scientific work packages 2-6 shall be consolidated for the regulatory authorities and other users as part of a "NANoREG Toolbox". The Toolbox, aims at providing the NANoREG stakeholders with a categorised collection of decision-supporting instruments for the short to medium term, useful in the European REACH legislative context, and possibly beyond.

This Toolbox does not 'end' with the tools produced by NANoREG. *It goes much further by scanning a wide horizon* made of test methods, datasets, models, guidance documents, decision trees, etc. produced by other (non)EU-funded projects, other initiatives in Europe and beyond, some supported by Industry rather than by national or international funding agencies.

2.2.1 Identification of the concept of 'Tool' in NANoREG

T1.7 has considered clarifying the concept of 'tool' compared to the project DoW. Actually, this any many other reflections on key terms has been conducted also in the context of the creation of the 'NANoREG harmonised terminology', which is Annex I of the NANoREG Framework (D1.11). The overall 'NANoREG definition' of tool adopted by T1.7 in collaboration with T1.4 during its work hence is:

"A tool is an experimental or computerised procedure used to generate, collect and/or store a certain type of output".

2.2.2 Scope and organisation of the NANoREG Toolbox

First of all, the NANoREG Toolbox contains tools developed or recommended / suggested by NANoREG partners of T1.7 and T1.4 for the safety assessment of nanomaterials (NMs) in the European REACH legislative context. These are, for instance, standard operation procedures (SOPs), test methods, decision trees, etc. These tools are also those mentioned in the work done by task 1.3 on 'Scientific answers to regulatory questions' (D1.9). They are closely related to the 'nano-specific' considerations of the NANoREG Framework document for addressing the safety assessment of NMs (task 1.4, D1.11). The 'safety in the value chain case studies' (SVCCSs) of task 1.6 also have been taken into account as far as possible.

Secondly, several other sources have been considered: relevant initiatives, past and present, by accessing them directly or through the scientific literature. They are (non)EU-funded projects, other activities in Europe and beyond, some supported by Industry rather than by national or international funding agencies. The T1.7 leader has thus conducted a rather wide and comprehensive horizon scanning to compile the Toolbox and make it as useful and complete as possible.

Structure of the Toolbox

The Toolbox has been structured, as was discussed with all partners of T1.7 and T1.4 at a workshop on 18 May 2016 in Amsterdam Schiphol. The tools are generally organized according to the logic of the NANoREG Framework document. The Excel[®] workbook, which represents the Toolbox, generally contains sheets named according to the topics (headers of the sections) of the Framework document. The Toolbox *mirrors* the Framework. Each worksheet is identified by the correspondent section number plus a short title that recalls the title and content of that section. There is a special sheet called 'Screening and Control Banding' that assembles in one overview those tools that actually cover at once several aspects (sections) of the Framework, and for which the restriction to a single sheet of the Toolbox (a single topic of the Framework) would have been unfair (see Table 1 below).

Table 1: The worksheets of the Toolbox Excel[®] workbook

Tab - About the NANoREG Toolbox	General info about the workbook, its contents, purpose and use
Tab 2 - EC Nano Definition	Tools that help to determine whether the material under investigation fulfils the current EC definition of a nanomaterial

	(particle number size distribution, VSSA)
Tab 3.1 - REACH Substance ID	Tools that help to determine the substance identity parameters for nanomaterials to be considered under REACH (particle number size distribution, shape, aspect ratio, surface chemistry)
Tab 3.2 - REACH Info Requirements	Tools that help to determine physicochemical, toxicological and ecotoxicological parameters according to the current standard information requirements of REACH
Tab 3.3 - REACH Adaptation Rules	Tools that help to apply adaptation rules in REACH Annex XI (grouping, read-across, QSAR, WoE) to nanomaterials
Tab 3.4 - REACH Hazard assessment	Tools that help to identify and assess hazard of nanomaterials according to REACH requirements (including DNEL/DMEL and PNEC derivation)
Tab 3.5 - REACH Exposure assessment	Tools that help to define exposure scenarios and assess exposure to nanomaterials according to REACH requirements (including environmental, occupational, and consumer exposure)
Tab 3.6 - REACH Risk characterisation	Tools for risk characterisation according to REACH requirements (including environmental, occupational, and consumer risk)
Tab 4 - Nano-specific risk assessment	Tools for risk assessment of nanomaterials beyond the scope of REACH requirements
Tab 5 - Safe-by-design	Tools that help to implement the safe-by-design concept for nanomaterials
Tab 6 - Life Cycle Assessment	Tools that help to apply LCA to the nanomaterials case
Tab - Screening and Control Banding	Tools that in their implementation relate to several of the other tabs

This NANoREG deliverable 'Toolbox – D1.12' contains relevant tools that are *ready for use and declared available by their creators and accessible* at the time of its publication (end February 2017). For the T1.7 and T1.4 partners this was seen as a further guarantee of quality of this key output, and a way to ensure a good degree of usefulness for the project stakeholders and the wider nanoEHS community. This verification of existence, availability, functioning and accessibility of each tool has been performed by JRC.

This work was conducted to the best of JRC's ability and on own initiative. Hence, necessary disclaimers do apply for possible unintentional errors or incomplete verifications in a few cases.

T1.7 and its leader also kept an eye on tools that are not yet ready or available, but which are nonetheless known to be under development and likely to be released in 2017. This has led to the creation of a second 'box' and Excel® workbook called '*prospective tools*'.

The NANoREG Toolbox and the Prospective Toolbox are thus places where tools generated within NANoREG and elsewhere are *fully referenced* and enriched with *useful metadata* (see 2.2.3 below). Not only are the boxes accessible to the NANoREG stakeholders as two separate Excel® workbooks, but they will be so for the general public by the end of the project.

2.2.3 How tools are reported

The NANoREG Toolbox is not just a review work resulting in a 'list of tools'. As described above (see 2.2.2), the findings of this wide scanning exercise, within and outside the project, are enriched with useful metadata.

The Toolbox has the form of two Excel® workbooks (see 2.2.2): one for the actual Toolbox and one for the 'prospective tools'. Each workbook contains named worksheets (tabs) according to the sections of the NANoREG Framework (D1.11). One tool is reported per row in a worksheet. Several metadata parameters are recorded during the data entry, also using pre-filled drop-down menus:

- Purpose (What is the tool for?),
- Name of the tool, if any,
- Type of tool (see 2.2.4 below),

- Regulatory status of the tool (see 2.2.5 below),
- Verbal description of what the tool is and what it does,
- Documented applications of the tool (references), if any,
- Other information, if any,
- Project or organisation acting as developer or maintainer of the tool,
- Reference(s), scientific paper(s), report(s), etc. addressing this tool in particular,
- Web link to a relevant website where the tool is available, if any.

2.2.4 Proposed 'types' of tools

Bearing in mind the NANoREG definition of tool (see 2.2.1 above) and the variety of outputs that NANoREG has generated, JRC has identified the following 'types of tools' for the Toolbox, which were endorsed by T1.7-T1.4 during the Amsterdam workshop of 18 May 2016:

- *Experimental protocol*, for instance a protocol or guideline or SOP on how to conduct a certain toxicological experiment or how to characterise a certain physicochemical property,
- *Model*, such as a predictive algorithm of exposure or release into the environment or a (Q)SAR application,
- *Decision support tool*, e.g. a checklist or decision tree that helps the user to define a testing strategy based on a set of criteria, a software system providing the user with relevant information to be considered in decision-making,
- *Guidance*, i.e. a document prepared by an authority with the purpose of communicating official recommendations on how to implement specific regulatory requirements, such as ECHA guidance for implementation of REACH,
- *Report*, i.e. a document prepared by a research group or a public authority that gives independent advice on how to perform specific research activities or implement specific regulatory requirements,
- *Database*, i.e. a system to manage data and information.

Tools listed in the Toolbox must be *publicly available*. The use of a tool may require registration, and a tool may also be a commercial product (e.g. downloadable commercial software).

For the sake of clarity, '*What is not a tool*' has also been identified. The following items are not considered tools in the context of this Toolbox:

- Services provided for instance by consultants (usually against payment), even if they follow a specific procedure;
- Technical instruments for making measurements, or instructions for their use not concerning measurements that address engineered nanomaterials specifically.

2.2.5 Estimated regulatory status of a tool

Each tool is characterised by a '*regulatory status*'. With this concept JRC intended to refer to the status of the tool from a regulatory point of view, which aims at giving an indication of the tool's level of regulatory acceptance. For example, a tool that is still at a conceptual stage or has been proposed in literature, but has not been tested on real cases or undergone a formal validation procedure, usually is less acceptable in a regulatory process (e.g. to produce data for a REACH registration dossier) than a validated or standardised tool. To describe the regulatory status of a tool, the following options were identified:

- *Research product*: the tool is a research outcome that has not been tested/validated/standardised for regulatory purposes,
- *Validated*: the tool has undergone a formal validation procedure, so that data generated by the tool are accepted and ranked high in a regulatory context (note that limited validation, e.g. within one laboratory or with a small dataset, does not qualify the method as validated in the context of this Toolbox),
- *Harmonised*: the tool has undergone a formal harmonisation process at OECD level, so data generated by the tool are accepted and ranked high in a regulatory context,

- *Standardised*: the tool has undergone a formal standardisation process at ISO or CEN level, so data generated by the tool are accepted and ranked high in a regulatory context,
- *Regulatory document*: the tool is a document developed by a regulatory/competent authority and it therefore has regulatory relevance.

The proposed '*regulatory status*' qualifier and its estimation for each tool was a task performed by JRC. This assessment was been done to the best of JRC's ability on own initiative. Hence, necessary disclaimers do apply for possible unintentional errors or incomplete verifications.

2.3 Results

The results of the wide scanning exercise conducted by JRC and T1.7 are contained in the attached two Excel® workbooks: one for the *Toolbox* and one for the *Prospective tools*. Figure 1 below is a snapshot of a typical worksheet of the *Toolbox*.

In total, the *Toolbox* contains about 160 unique tools, of which about 40% were produced by NANoREG. The largest group of tools consists of exposure assessment tools (49 tools). The most common type of tool is the experimental protocol (56 tools), which is also the most common type of NANoREG product (48 tools). The prospective tools file contains 30 unique tools, of which again about 40% were produced by NANoREG.

Those tools are indeed addressing one or more aspects of the safety assessment of nanomaterials, generally in the REACH context. At the time of the end of the compilation work (February 2017) the tools listed were found to be available, accessible and functioning.

Figure 1: Example screenshot showing some of the tools listed in the *Toolbox* workbook.

WORKSHEET 2: Available tools for the implementation of the EC Definition of a nanomaterial - Linked to Section 2 of the NANoREG Framework								
What is the tool for?	Name	Type	Regulatory status	Description	Documented applications	Other information	Project/organisation	Pu
Measuring Particle Number Size Distribution	ISO TC 229 Nanotechnologies	Guidance	Standardised	List of standards concerning nanotechnologies under the direct responsibility of ISO/TC 229 Secretariat			ISO	
Measuring Particle Number Size Distribution	OECD Guidance Document. Applicability of OECD Test Guidelines to manufactured nanomaterials	Guidance	Regulatory document	Most OECD test guidelines (TGs) are suitable for MNs, but in some cases adaptations may be needed to address certain nano specificities. The OECD test guidelines programme has started to work on adapting some specific test guidelines to nanomaterials as well as to develop specific test guidelines and guidance documents for nanomaterials, which will lead to future regulatory test guidelines for MNs.			OECD	OE Gu Ma En Se Na On
Measuring Particle Number Size Distribution	ECHA Guidance for implementation of REACH. Recommendations for nanomaterials	Guidance	Regulatory document	ECHA guidance document that provides nanomaterial-specific recommendations for measuring particle number size distribution in order to fulfil REACH information requirements.			ECHA	EC red Ap na En Ag
Measuring Particle Number Size Distribution	Requirements on measurements for the implementation of the EC Definition	Report	Regulatory document	Report on requirements on measurements for the implementation of the European Commission definition of the term 'nanomaterial'.			JRC	Lin Ro on the test EU En
Measuring Volume Specific Surface Area (VSSA)	Towards a review of the EC Recommendation for a definition of the term 'nanomaterial'	Report	Regulatory document	Report on practical experience gathered in implementing the European Commission's Recommendation for a definition of the term 'nanomaterial'.			JRC	Ro res die Act the an OF
Providing nanomaterials for testing	BAM Reference Materials	Repository	Not applicable	Repository for certified nanoscaled reference materials			BAM/ISO	
Providing nanomaterials for testing	JRC Repository of Nanomaterials	Repository	Not applicable	The JRC hosts a repository of representative industrial nanomaterials (NMs), including nanomaterials studied in the OECD testing programme and large research projects. Each type of material in the repository has been sourced as a large single batch			JRC	

2.4 Evaluation and conclusions

Although the tools generally address the European REACH regulatory context, several of them are worth considering in other safety assessment strategies applicable to nanomaterials.

This Toolbox likely constitutes a first-time large and rather complete collection of categorised, well described and actual tools from a wide review, which extends well beyond the large EU-funded project NANoREG.

The resulting two large Excel[®] worksheets list categorised tools, with descriptive information and metadata attached to them (in the worksheet rows). As such, D1.12 is a precious dataset, available to the global nanoEHS community, be it regulators or industry, ready for further expansion and exploitation.

Making the use of the dataset user-friendlier than an Excel[®]-based system was unfortunately not within reach of T1.7 or JRC due to limited resources available. As suggestion for the future users and further developers of the Toolbox, it should be rather simple to turn this Excel[®]-based dataset into a Wiki-like set of webpages for easy access and browsing.

Just like the Framework, this large Toolbox will be eventually publicly available at the end of the project (end February 2017). The Excel[®] files will be linked to a unique literature identifier in early March 2017, so that they can be easily referenced to by those who wish to exploit them. This Toolbox is also a building block for the White Paper of the EU-funded Horizon 2020 project ProSafe.

2.5 Data management

Not applicable

3 Deviations from the work plan

The work of task 1.7 and the related production of this deliverable proceeded as quickly as possible, but, obviously, not faster than the actual production of NANoREG tools. Great efforts were however made to release this important NANoREG output as soon as possible (earlier than the amended deadline of M48) and close to the original foreseen date of M42 (01/09/2016).

4 References / selected sources of information

The many sources of information used for this deliverable are reported in the Toolbox Excel[®] files, next to each identified tool.

Annexes

The bulk of this deliverable consists of two attached Excel[®] files:

- A workbook containing the presently existing and usable tools, *the Toolbox* (NANoREG-ToolBox-v11_D1.12_final.xlsx),
- A workbook containing '*prospective tools*', the actual existence and usability of which could not be (fully) ascertained by the date of final release of this deliverable (end February 2017) (NANoREG-Prospective tools-v5_D1.12_final.xlsx).

-oOo-