



The EU FP7 NanoDefine Project

Development of an integrated approach based on validated and standardized methods to support the implementation of the EC recommendation for a definition of nanomaterial

Review of existing calibration or reference materials

NanoDefine Technical Report D1.1

Andreas F. Thünemann, Franziska Emmerling and Vasile-Dan Hodoroaba

The NanoDefine Consortium 2014

NanoDefine in a nutshell

The EU FP7 NanoDefine project was launched in November 2013 and will run until October 2017. The project is dedicated to support the implementation of the EU Recommendation on the Definition of Nanomaterial by the provision of the required analytical tools and respective guidance. Main goal is to develop a novel tiered approach consisting of (i) rapid and cost-efficient screening methods and (ii) confirmatory measurement methods. The "NanoDefiner" eTool will guide potential end-users, such as concerned industries and regulatory bodies as well as enforcement and contract laboratories, to reliably classify if a material is nano or not. To achieve this objective, a comprehensive inter-laboratory evaluation of the performance of current characterisation techniques, instruments and software is performed. Instruments, software and methods are further developed. Their capacity to reliably measure the size of particulates in the size range 1-100 nm and above (according to the EU definition) is validated. Technical reports on project results are published to reach out to relevant stakeholders, such as policy makers, regulators, industries and the wider scientific community, to present and discuss our goals and results, to ensure a continuous exchange of views, needs and experiences obtained from different fields of expertise and application, and to finally integrate the resulting feedback into our ongoing work on the size-related classification of nanomaterials.

Bibliographic data

NanoDefine Technical Report D1.1

Report title: Review of existing calibration or reference materials

Author: Thünemann A. F.* , Emmerling F. and Hodoroaba V.-D.

Affiliation: Bundesanstalt für Materialforschung und Prüfung (BAM), Unter den Eichen 87, 12205 Berlin, Germany

Publication date: 26/06/2014

Publisher: The NanoDefine Consortium

© Copyright 2014: The NanoDefine Consortium

Place of publication: Wageningen, the Netherlands

Citation: Thünemann A. F., Emmerling F. and Hodoroaba V.-D.: Review of existing calibration or reference materials, NanoDefine Technical Report D1.1, NanoDefine Consortium, Wageningen, 2014

URL: <http://www.nanodefine.eu>

Contact: coordinator@nanodefine.eu, www.nanodefine.eu

* Corresponding author: andreas.thuenemann@bam.de

Table of Contents

| | | |
|-----|---|----|
| 1 | Abbreviations and acronyms..... | 5 |
| 2 | Summary | 6 |
| 3 | Introduction | 7 |
| 4 | Calibration and Reference Materials..... | 8 |
| 4.1 | Database Nanoscaled Reference Materials..... | 12 |
| 4.2 | Literature reviews of Nanoscaled Reference Materials..... | 12 |
| 4.3 | Non-Certified Nanoscaled Materials | 14 |
| 4.4 | Reference Materials from other EU Projects..... | 16 |
| 5 | Conclusions | 17 |
| 6 | References | 18 |

Index of figures

- Figure 1:** Theoretical example of a bi-modal size distribution of particles of 20 nm and 200 nm size – as sketched simplified for four particles in the mid of the diagram. Whereas the 50-50% number weighted size distribution (in red) defines the material as a nano-material, note that the corresponding volume weighted size distribution (in blue) provides an almost invisible contribution of the 20 nm particles.7
- Figure 2:** Nano-objects of interest for NanoDefine (Stefaniak et al., 2013). 13

Index of Tables

- Table 1:** List of certified reference materials (CRM)9
- Table 2:** List of reference materials (RM) 11
- Table 3:** List of representative test material (RTM) 15
- Table 4:** Survey from the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013) with the nano reference materials considered in the specific project. 16

1 Abbreviations and acronyms

| | |
|-----------|--|
| BAM | Federal Institute for Materials Research and Testing |
| BET | Brunauer-Emmet-Teller Specific Surface Area |
| CD | Committee Draft |
| CLS | Centrifuge Liquid Sedimentation |
| COMAR | International Database for Certified Reference Materials |
| CRM | Certified Reference Material |
| ENP | Engineered Nanoparticles |
| ICP-MS | Inductively Coupled Plasma Mass Spectrometry |
| IHCP | JRC Institute for Health and Consumer Protection |
| INAA | Instrumental Neutron Activation Analysis |
| ISO | International Organization for Standardization |
| ISO/REMCO | Committee on Reference Materials |
| IRMM | Institute for Reference Materials and Measurements |
| JRC | Joint Research Centre |
| JSR | JSR Corporation (Japan) |
| MP | Micromod Partikeltechnologie GmbH (Germany) |
| MWCNTs | multi-wall carbon nanotubes |
| NIM | National Institute of Metrology (China) |
| PGAA | Neutron Prompt Gamma Activation Analysis |
| QCM | Quality Control Material |
| RM | Reference Material |
| RTM | Representative Test Material |
| SNP | Silica Nanoparticles |
| TC | Technical Committee |
| VL SI | VL SI Standards, Inc. (USA) |
| WD | Working Draft |

2 Summary

We report on calibration standards of nanoparticles meeting the definition of a nano-material given by the European Commission (EU 2011) which are relevant for the characterisation methods applied in the NanoDefine project. We found that the impact of nanoparticles is outstanding in the scientific literature. A number of 270.000 paper titles on nanoparticles are listed in the Web of Science data base. But surprisingly, the availability of suitable certified standard reference materials is scarce. Only a few sources were found. For example, BAM provides the database Nanoscaled Reference Materials at <http://www.nano-refmat.bam.de/en/> in cooperation with the ISO/TC 229 Nanotechnologies. In addition, two publications from 2013 on nanoscale reference materials are available.

Candidates of nano-(certified) reference materials from other ongoing or just finished FP6 and FP7 nano-metrology projects have been extracted from the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013). Recommendations for selection of representative test materials and calibration standards for NanoDefine internal tasks, respectively, are also given.

3 Introduction

The task of this deliverable is to review the availability of relevant materials at metrology institutes, commercial suppliers, and research institutes as well as past and present projects. Focus will be on information newly available since the proposal drafting. The suitability of materials for the purposes of the definition will be evaluated and recommendations given to other NanoDefine tasks.

One relevant issue with respect to the application of these selected materials to the scope of NanoDefine is also the need of consideration of existing calibration or reference materials of sizes which are larger than 100 nm. In the present compilation “non nano” materials with sizes of hundreds of nm up to μm range are separately listed, too. The sense of consideration of non-nano materials for the purpose of NanoDefine can be probably best argued by giving an example: let’s assume that the measured particle size distribution of a material shows 50% of particles of 20 nm size and the other 50% at 200 nm, see Figure 1. According to the EC recommendation this material must be categorized as a nano-material. A slightly higher proportion of the 200 nm particles will “transform” the nanomaterial into non-nanomaterial. Hence, the accurate evaluation of particles also well above 100 nm based on (C)RMs compiled here is decisive in the exercise of determining if a material is nano or non-nano. Consideration of (C)RMs with primary particles of sizes in the μm range and more are practically not significant for the application of the recommendation. Already for the example above of 50-50% number weighted particles of 20 and 200 nm respectively, the volume weighted ratio is 203 to 2003, i.e. one per mille particles of sizes below 100 nm. The 20 nm peak in the volume sizes distribution in Figure 1 can be barely observed. Larger particles in the same number proportion of 50 to 50% to the 20 nm ones will bring the volume weighted ratio even well below one per mille, i. e. really extreme in practice.

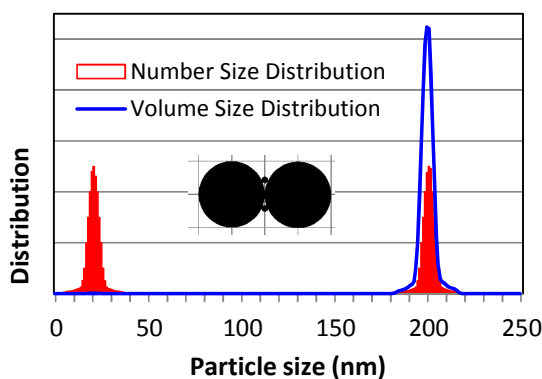


Figure 1: Theoretical example of a bi-modal size distribution of particles of 20 nm and 200 nm size – as sketched simplified for four particles in the mid of the diagram. Whereas the 50-50% number weighted size distribution (in red) defines the material as a nano-material, note that the corresponding volume weighted size distribution (in blue) provides an almost invisible contribution of the 20 nm particles.

4 Calibration and Reference Materials

Reference materials (RMs) are essential for the improvement and maintenance of a worldwide coherent measurement system. RMs with different characteristics are of central importance in method validation. Details are provided in the ISO Guide 35. It should be noted that a hierarchy of reference materials exists (G. Roebben et al. 2013):

- **Certified Reference Material (CRM):** A certified reference material is a reference material characterised by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability.
- **Reference Material (RM):** A reference material is a material, sufficiently homogeneous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process.
- **Representative Test Materials: (RTM)** A representative test material (RTM) is a material from a single batch, which is sufficiently homogeneous and stable with respect to one or more specified properties, and which implicitly is assumed to be fit for its intended use in the development of test methods whose target properties are other than the properties for which homogeneity and stability have been demonstrated.

We found five sources of relevance providing information about the availability of reference materials and representative test materials:

- BAM website in collaboration with ISO/TC 229 Nanotechnologies (“Nanoscale reference materials”),
- COMAR international database for certified reference materials,
- A recent paper from Stefaniak et. al. (Stefaniak, Hackley, Roebben, Ehara, Hankin, Postek, Lynch, Fu, Linsinger, and Thünemann 2013) entitled “Nanoscale reference materials for environmental, health and safety measurements: needs, gaps and opportunities”,
- A recent paper from Orts-Gil et. al. (Orts-Gil, Natte and Österle 2013) entitled “Multi-parametric reference nanomaterials for toxicology: state of the art, future challenges and potential candidates”, and
- The Nanomaterial Repository of JRC Institute for Health and Consumer Protection (IHCP).

An extract of these sources can be found in the Tables 1, 2 and 3.

Furthermore, candidates of nano-(certified) reference materials from other ongoing or just finished FP6 and FP7 nano-metrology projects have been surveyed from the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013) and presented in Table 4.



| Description | Name | Reference or certified value ¹⁾ | Method ²⁾ | Provider | Source | Suitability to NanoDefine |
|---|-----------|---|-------------------------|----------|-----------------|---------------------------|
|  | | | | | | |
| Nano | | | | | | |
| Silica | ERM-FD100 | 20 nm size | DLS; CLS; TEM/SEM; SAXS | IRMM | Orts-Gil et al. | Highly recommended |
| Silica | ERM-FD304 | 40 nm size | DLS; CLS | IRMM | Orts-Gil et al. | Highly recommended |
| Silver | BAM-N001 | 35 nm, d90, volume-weighted | SAXS | BAM | Orts-Gil et al. | recommended |
| SWCNTs | SRM 2483 | elemental composition | INAA; PGAA; ICP-MS | NIST | Orts-Gil et al. | recommended |
| TiO ₂ | SRM 1898 | 55.55 m ² /g specific surface area | BET | NIST | Orts-Gil et al. | recommended |
| Nano-Alumina | GBW 13901 | 445,4 m ² /g specific surface area | BET | NIM | Nano RefMat | |
| Non-Nano | | | | | | |
| Polystyrene | GBW 12031 | 482.9 – 491.6 nm | n/a | NIM | COMAR | |
| Polystyrene | GBW 12018 | 277.7 – 282.9 nm | n/a | NIM | COMAR | |
| Quartz | BCR-066 | 350 – 3500 nm | sedimentation analysis | IRMM | COMAR | |
| Silicon nitride | SRM 659 | 480 – 2800 nm | Sedigraph | NIST | COMAR | recommended |

Table 1: List of certified reference materials (CRM)

¹⁾ Values shown here are approximate since nominal size depends on experimental technique.

²⁾ Methods that were used for certification.

| Description | Name | Reference or certified value ¹⁾ | Provider | Source | Suitability to NanoDefine  |
|----------------------------------|----------------------------------|---|----------|-----------------|--|
| Nano | | | | | |
| Gold | RM 8011 | 10 nm | NIST | Orts-Gil et al. | Highly recommended |
| Gold | RM 8012 | 30 nm | NIST | Orts-Gil et al. | Highly recommended |
| Gold | RM 8012 | 60 nm | NIST | Orts-Gil et al. | Highly recommended |
| SWCNTs „bucky paper“ | RM 8282 ²⁾ | elemental composition | NIST | Orts-Gil et al. | |
| SWCNT | RM 8281 | 200, 400 and 800 nm length | NIST | Orts-Gil et al. | |
| Silver | RM 8016 ²⁾ | 10 nm | NIST | Orts-Gil et al. | recommended |
| Silver | RM 8017 ²⁾ | 75 nm | NIST | Orts-Gil et al. | recommended |
| Polystyrene particle | GBW 12011 | 61 nm | NIM | Nano RefMat | |
| polystyrene latex spheres | STADEX SC-0030-A, | 29 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | STADEX SC-0050-D | 48 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | STADEX SC-0055-D | 55 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | STADEX SC-0060-D | 61 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | SC-0070-D | 70 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | SC-0075-D | 76 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | SC-0080-D | 80 nm | JSR | Nano RefMat | recommended |
| polystyrene latex spheres | SC-0100-D | 100 nm | JSR | Nano RefMat | recommended |
| iron oxid in a matrix of dextran | nanomag®-D-spio particles 50 nm | 20 nm | MP | Nano RefMat | |
| iron oxid in a matrix of dextran | nanomag®-D-spio particles 50 nm | 50 nm | MP | Nano RefMat | |
| iron oxid in a matrix of dextran | nanomag®-D-spio particles 100 nm | 100 nm | MP | Nano RefMat | |
| Nano-Alumina | GBW 13906 | 359,4 m ² /g specific surface area | NIM | Nano RefMat | |
| Nano-Alumina | GBW 13907 | 515,3 m ² /g specific surface area | NIM | Nano RefMat | |
| Non-Nano | | | | | |

| | | | | | |
|--|-------------------------------------|---|-------|-------------|-------------|
| Size standard particles | CLINTEX 017-10K | 168 nm | JSR | Nano RefMat | |
| Polystyrene particle | GBW 12009 | 948 nm | NIM | Nano RefMat | recommended |
| Polystyrene particle | GBW 12010 | 352 nm | NIM | Nano RefMat | recommended |
| Silicon dioxide | GBW 12013 | 951 nm | NIM | Nano RefMat | recommended |
| Silicon dioxide | GBW 12014 | 458 nm | NIM | Nano RefMat | recommended |
| Silicon dioxide | GBW 12015 | 296 nm | NIM | Nano RefMat | recommended |
| Silicon dioxide | GBW 12016 | 143 nm | NIM | Nano RefMat | recommended |
| Titanium Dioxide (anatase) | NM-100 | 267 nm | JRC | Nano RefMat | recommended |
| silica spheres on Si wafer; Used to calibrate instruments which size and detect particles on the surface of bare silicon wafers | Silica Contamination Standard (SCS) | 100 nm, 126 nm, 150 nm, 180 nm | VL SI | Nano RefMat | |

Table 2: List of reference materials (RM)

¹⁾ Values shown here are approximate since nominal size depends on experimental technique.

²⁾ in production

4.1 Database Nanoscaled Reference Materials

The website of the BAM Nanotechnology Task Force provides a database Nanoscale Reference Materials at <http://www.nano-refmat.bam.de/en/> (BAM 2014). The database is established in collaboration with ISO/TC 229 Nanotechnologies and is a compilation of nanoscale reference materials worldwide available. Therein a list of categories is provided. Relevant for NanoDefine is the category nano-objects/nanoparticles/nanomaterials, see Tables 1 and 2.

In addition, the COMAR international database for certified reference materials (COMAR 2014) lists CRMs produced worldwide by about 220 producers in 25 countries. The web site can be found at <http://www.comar.bam.de/en/>. It is necessary to register for using the charge-free COMAR database. A number of 10356 CRMs are listed in COMAR. Unfortunately, nanomaterials and nanoparticles are not listed yet as a separate category in COMAR. A search in the category "Physical Property" after "Particle Size" and adding "nm" Unit as a supplementary "Physical property" results in a list with 28 reference materials.

4.2 Literature reviews of Nanoscaled Reference Materials

A recent review entitled "Nanoscale reference materials for environmental, health and safety measurements: needs, gaps and opportunities" (Stefaniak et al., 2013) lists nano-objects which are also relevant for NanoDefine, see Figure 2. Five lists were identified that contained 25 (classes of) nano-objects; only four nano-objects (gold, silicon dioxide, silver, titanium dioxide) appeared on all lists. Twenty-three properties were identified for characterisation; only (specific) surface area appeared on all lists. The key themes that emerged from this review were:

- Various groups have prioritised nano-objects for development as "candidate RMs" with limited consensus;
- A lack of harmonised terminology hinders accurate description of many nano-object properties;
- Many properties identified for characterisation are ill-defined or qualitative and cannot be measured in a metrologically traceable manner;
- Standardised protocols are critically needed for characterisation of nano-objects as delivered in relevant media and as administered to toxicological models;
- The measurement processes being used to characterise a nano-object must be understood because instruments may measure a given sample in a different way;
- Appropriate RMs should be used for both accurate instrument calibration and for more general testing purposes (e. g., protocol validation);
- There is a need to clarify that where RMs are not available, if "(representative) test materials" that lack reference or certified values may be useful for toxicology testing and
- there is a need for consensus building within the nanotechnology and environmental, health and safety communities to prioritise RM needs and better define the required properties and (physical or chemical) forms of the candidate materials.

Table 1. Nano-objects of interest as nanoscale reference materials for risk assessment*.

| NIST (2007) [†] | REFNANO [‡] | OECD (2010) [§] | NanoImpactNet [§] | NanoValid [‡] |
|--------------------------|----------------------------------|--------------------------|----------------------------|------------------------|
| Dendrimers | Carbon black | Aluminium oxide | Polystyrene (f) | Copper oxide |
| Fullerenes | Combustion-derived | Cerium oxide | Silver | Fullerenes |
| Gold | Metals and their oxides (Cu, Fe) | Dendrimers | Titanium dioxide | Gold |
| Isotope labelled | MWCNT | Fullerenes | Combustion-derived | MWCNT |
| Metal oxides (Ce, Fe) | Polystyrene (f) | Gold | Copper/copper oxides, iron | Palladium |
| MWCNT | Silver | Iron | Fullerenes | Silicon dioxide |
| Quantum dots | SWCNT | MWCNT | Gold | Silver |
| Silicon dioxide (a, c) | Titanium dioxide | Nanoclays | Silicon dioxide | SWCNT |
| Silver (p, i) | Zinc oxide | Silicon dioxide | | Titanium dioxide |
| SWCNT | Gold | Silver | | Zinc oxide |
| Titanium dioxide | Cerium oxide | SWCNT | | Calcium phosphate salt |
| | Silicon dioxide | Titanium dioxide | | Cerium oxide |
| | Ceramics | Zinc oxide | | Ceramics |
| | Rods, cubes, horns | | | Dendrimers |
| | Isotope labelled | | | Lead phosphate salt |
| | Nanoclays | | | Nanocellulose |
| | | | | Nanoclays |
| | | | | Quantum dots |
| | | | | Polystyrene |

*f = fluorescent; MWCNT = multi-walled carbon nanotubes; SWCNT = single-walled carbon nanotubes; a = amorphous; c = crystalline; p = particulate; i = ionic; †Nano-objects are listed without any implied priority; ‡REFNANO: high priority materials are listed above the single horizontal line (listed alphabetically with no relative priority implied) and low priority materials are listed below the thick line in assigned order of priority (Aitken et al. 2008); §Nano-objects are listed without any implied priority; §NanoImpactNet: Materials above single thick horizontal line were agreed upon by all three workshop discussion groups; materials between thick single horizontal line and thick double horizontal line were agreed upon by one or more but not all workshop groups; materials below thick double horizontal line were added based on perceived needs of ecotoxicology community. Within each grouping, materials are listed alphabetically with no relative priority implied (Stone et al. 2010); ‡NanoValid: Priority 1 materials are listed above the single horizontal line and Priority 2 materials are listed below the line; within each grouping, materials are listed alphabetically with no relative priority implied (Reuther 2011).

Figure 2: Nano-objects of interest for NanoDefine (Stefaniak et al., 2013)

Furthermore, a review and perspective paper has been given by Orts-Gil et al. (Orts-Gil et al., 2013) entitled “Multi-parametric reference nanomaterials for toxicology: state of the art, future challenges and potential candidates”. In that contribution the authors review available RMs, see Table 2, ongoing projects and characterisation trends in the field. The conclusion is that actual approaches to RMs mostly deal with metrological considerations about single properties of the ENPs, typically their primary particle size, which can hardly be representative of nanoparticles characteristics in real testing media and therefore, not valid for reliable and comparable toxicological studies. As an alternative, we discussed the convenience and feasibility of establishing multi-parametric RMs for a series of ENPs, focusing on silica nanoparticles (SNPs). As a future perspective, the need to develop RMs based on hybrid nanoparticles is also discussed.

4.3 Non-Certified Nanoscaled Materials

- Nanomaterial Repository of JRC Institute for Health and Consumer Protection (IHCP) offers representative nanomaterials to support international collaborative studies (see web site http://ihcp.jrc.ec.europa.eu/our_activities/nanotechnology/nanomaterials-repository).
- The materials are listed in Table 3.
- Many companies offer different types of nanomaterials; only a few will be mentioned:
 - Nanosphere Size STDS 100 nm, DUKE-3100A (offered from LGC Standards)
 - Particles with different (bio)organic or inorganic matrix materials are offered by Micromod Partikeltechnologie GmbH (Germany)
 - Sigma Aldrich offers different types of nanopowders and dispersions, gold nanoparticles, quantum dots and much more (<http://www.sigmaaldrich.com/materials-science/nanomaterials.html>)

| Description | Name | Mean particle size | Primary particle or crystal size | Provider | Suitability to NanoDefine |
|--|-------------------------|--------------------|----------------------------------|----------|---------------------------|
| Titanium Dioxide, anatase | NM-100* | 267 nm | 42 - 90 nm | JRC | recommended |
| Titanium Dioxide, anatase | NM-101* | 38 nm | 6 nm | JRC | recommended |
| Titanium Dioxide, anatase | NM-102* | 132 nm | 20 nm | JRC | recommended |
| Titanium Dioxide thermal, hydrophobic, rutile | NM-103* | 186 nm | 20 nm | JRC | recommended |
| Titanium Dioxide thermal, hydrophilic, rutile | NM-104* | 67 nm | 20 nm | JRC | recommended |
| Titanium Dioxide rutile-anatase | NM-105* | 95 nm | 22 nm | JRC | recommended |
| Zinc Oxide, uncoated | NM-110* | 150 nm | 42 nm | JRC | recommended |
| Zinc Oxide coated triethoxycaprylsilane | NM-111* | 140 nm | 34 nm | JRC | |
| Synthetic Amorphous Silica PR-A-02, precipitated | NM-200* | 47 nm | 20 nm | JRC | |
| Synthetic Amorphous Silica PR-B-01, precipitated | NM-201* | 62 nm | 8-15 nm | JRC | |
| Synthetic Amorphous Silica PY-AB-03, thermal | NM-202* | 108 nm | 8-15 nm | JRC | |
| Synthetic Amorphous Silica PY-A-04, thermal | NM-203* | 137 nm | 8-20 nm | JRC | |
| Synthetic Amorphous Silica PR-A-05, precipitated | NM-204* | 75 nm | 8-15 nm | JRC | |
| Cerium Dioxide | NM-211 [#] | n/a | | JRC | |
| Cerium Dioxide | NM-212 [#] | n/a | | JRC | |
| Silver | NM-300K [#] | n/a | | JRC | |
| Silver dispersant | NM-300 DIS [#] | n/a | | JRC | |
| Gold | NM-330 [#] | n/a | | JRC | |
| Gold-dispersant | NM-330 DIS [#] | n/a | | JRC | |

| | | | | | |
|---|---------------------|-----------------|--|-------------------------------------|--|
| MWCNT | NM-400 [#] | n/a | | JRC | |
| MWCNT | NM-401 [#] | n/a | | JRC | |
| MWCNT | NM-402 [#] | n/a | | JRC | |
| MWCNT | NM-403 [#] | n/a | | JRC | |
| Nanoclay | NM-600 [#] | n/a | | JRC | |
| Nanosphere Size STDS 100 nm | DUKE 3100A | 100 nm | | LGC Standards | |
| particles with different (bio)organic or inorganic matrix materials | | 10 – 100 000 nm | | MP | |
| SiO ₂ nanoparticles CRM candidate from FP7 project <i>NanoValid</i> | Lys-SNPs-B1 | 15 nm | | BAM (has to be confirmed) | |
| Gold, silver nanoparticles CRM candidate from FP7 project INSTANT | n/a | < 50 nm | | (has to be confirmed and specified) | |

Table 3: List of representative test material (RTM)

^{*}List of materials in the JRC Nanomaterials (NM) Repository (2011/2013)

[#]List of representative nano-materials in the JRC NM Repository (2013) taken from the JRC Scientific and Policy Report: Synthetic Amorphous Silicon Dioxide (NM-200, NM-201, NM-202, NM-203, NM-204): Characterisation and Physico-Chemical Properties

4.4 Reference Materials from other EU Projects

Reference materials are also produced in further EU projects as indicated in Figure 2. For instance in the project ENNSATOX (<http://www.ennsattox.eu>) SiO₂, ZnO, TiO₂, of different shapes, sizes and dimensions are produced. Different nanoparticle reference materials are produced in the FP7 Project INSTANT (<http://www.instant-project.eu/index.php?id=22>). In principle, CRM candidates of silver, gold, etc. nanoparticles are available from INSTANT. Diameters of these particles are in the range significant smaller than 50 nm.

As far as the FP7 project NanoValid is concerned (<http://www.nanovalid.eu/>), a suitable nano-CRM candidate has been proven to be the sample Lys-SNPs-B1 (“BAM silica”), which consists of SiO₂ nano-particles almost monodisperse and of approximately 15 nm size.

Reference materials are also produced in further projects as indicated in Figure 2 and Table 4 on the basis of the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013).


| Project | Nano-RM considered | Suitability to NanoDefine |
|-------------|--|---|
| | |  |
| ENPRA | TiO ₂ , MWCNT ENPs | yes |
| INSTANT | Ag, Au, etc. | yes |
| MARINA | TiO ₂ , SiO ₂ , Ceria Oxide, ZnO, nanoAg | yes |
| ModNanoTox | Ag | yes |
| NANODEVICE | SWCNT | yes |
| Nanalyse | metal, metal oxide/silicate, carbon and organic ENP, gelatine NP | |
| NANOMICEX | ZnO, CoAl ₂ O ₄ , TiO ₂ , Al ₂ O ₃ | yes |
| NanoValid | metal oxides (SiO ₂ , TiO ₂ , ZnO, CuO), metals (Ag, Au and Pd), CNTs (SWCNTs and MWCNTs) and fullerenes; quantum dots (CdSe, CdS, CeO ₂), salts (Ca-phosphates, PbS), nanocellulosic materials, polystyrene, dendrimers, ceramics, nanoclays. SiO ₂ , Ag | yes |
| QualityNano | ERM FD100 | yes |
| SANOWORK | “reference benchmark materials” | |

Table 4: Survey from the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013) with the nano reference materials considered in the specific project

5 Conclusions

A brief and concise review on calibration or reference materials of nanoparticles in a size range relevant for the characterisation methods used in the NanoDefine project is given. The impact of nanoparticles is outstanding in the scientific literature. In spite of the huge number of publications dealing with nanoparticles there is a surprisingly small number of available certified standard reference materials which are available. Only a few sources were found. For example, BAM provides in cooperation with the ISO/TC 229 Nanotechnologies the database Nanoscaled Reference Materials (BAM 2014). Furthermore, two recent review publications on Nanoscale reference materials are discussed with the focus on the newest reference materials and the problems and trends at the practical use of the available reference nanomaterials.

A survey on the nano-(certified) reference materials considered by other ongoing or just finished FP6 and FP7 nano-metrology projects has been made based on the Compendium of Projects in the European NanoSafety Cluster (Compendium NSC, 2013). The majority of the materials involved or to be developed is well represented in the materials selected already in NanoDefine for other tasks. The need of certified reference materials with sizes significantly below 50 nm can be pointed out. Suitable materials for other NanoDefine tasks besides the already selected 14 representative test materials would be e.g. the SiO₂ samples (Lys-SNPy-B1).

6 References

- BAM, <http://www.nano-refmat.bam.de/en/> (accessed 11/02/2014).
- COMAR International database for certified reference materials, <http://www.comar.bam.de/en/> (accessed 11/02/2014), registration is necessary to access the database.
- Compendium of Projects in the European NanoSafety Cluster – 2013 edition. Michael Riediker and (Ed.) Lausanne, Switzerland: Institute for Work and Health 2013 — 274 pp. — 21 x 29.7 cm.
- JRC IHCP http://ihcp.jrc.ec.europa.eu/our_activities/nanotechnology/nanomaterials-repository (accessed 12/02/2014).
- EC/FP7 project INSTANT, <http://www.instant-project.eu/index.php?id=22> (accessed 11/02/2014).
- EC (European Commission) (2011) Commission Recommendation of 18 October 2011 on the definition of nanomaterial (2011/696/EU). OJ L 275, 20.10.2011, 38–40
- ISO/WD Guide 35 Reference materials -- General guidance for the value assignment of property values, WD approved for registration as CD, www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=60281 (accessed 11/02/2014).
- EC/FP7 project NanoValid, <http://www.nanovalid.eu/> (accessed 21/02/2014).
- Orts-Gil, G., Natte, K., Österle, W., 2013. Multi-parametric reference nanomaterials for toxicology: state of the art, future challenges and potential candidates. *RSC Advances* 3:18202-18215.
- Stefaniak, A.B., Hackley, V.A., Roebben, G., Ehara, K., Hankin, S., Postek, M.T., Lynch, I., Fu, W.-E., Linsinger, T.P.J., Thünemann, A.F., 2013. Nanoscale reference materials for environmental, health and safety measurements: needs, gaps and opportunities. *Nanotoxicology* 7:1325-1337.
- G. Roebben, K. Rasmussen, V. Kestens, T.P.J. Linsinger, H. Rauscher, H. Emons, H. Stamm, 2013. Reference materials and representative test materials: the nanotechnology case. *J. Nanopart. Res.* 15:1455