

**ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY
ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY**

**INVESTIGATING THE DIFFERENT TYPES OF RISK ASSESSMENTS OF
MANUFACTURED NANOMATERIALS**

**IDENTIFYING TOOLS AVAILABLE FOR RISK MANAGEMENT MEASURES AND
UNCERTAINTIES DRIVING NANO-SPECIFIC DATA NEEDS**

**Series on the Safety of Manufactured Nanomaterials
No. 88**

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IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

**Environment Directorate
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
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This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organisations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

The OECD Working Party on Manufactured Nanomaterials (WPMN) is a subsidiary body of the OECD Chemicals Committee. This programme concentrates on human health and environmental safety implications of manufactured nanomaterials (limited mainly to the chemicals sector), and aims to ensure that the approach to hazard, exposure and risk assessment is of a high, science-based, and internationally harmonised standard. It promotes international co-operation on the human health and environmental safety of manufactured nanomaterials, and involves the safety testing and risk assessment of manufactured nanomaterials.

This document presents the findings from the survey conducted in 2016 which aimed at investigating the different types of risk assessment. The survey provided information on the scope and specific features of different regulatory risk assessments for manufactured nanomaterials by comparing and contrasting the conditions, assumptions, and levels of uncertainties of approaches used in countries.

This document is published under the responsibility of the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, pesticides and Biotechnology of the OECD.

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BACKGROUND

1. This project focuses on issues arising in risk assessment of nanomaterials including supporting the OECD Council Recommendation on the Safety Testing and Assessment of Manufactured Nanomaterials [C(2013)107; C/M(2013)16; ENV/JM(2017)3] (OECD, 2013_[11]), which concluded that “Members, to manage the risks of manufactured nanomaterials, apply the existing international and national chemical regulatory frameworks or other management systems, adapted to take into account the specific properties of manufactured nanomaterials.”

SOME OF THE QUESTIONS TO BE ASKED/DATA GATHERED

2. The survey was conducted to gather the following information concerning risk assessments in different member countries:
- Different types of risk assessment used by jurisdictions. For example:
 - Screening (i.e. risk and hazard prioritisation) level versus a more detailed risk assessment;
 - Level of detail in the assessment; and
 - Jurisdictions which emphasize hazard more than risk/exposure;
 - Levels of uncertainties/assumptions used in these risk assessments;
 - Risk management measures and other outcomes of the assessment; and
 - Risk assessment process (es) used when evaluating manufactured nanomaterials including uncertainties, data requirements, and characterization/identification.

OUTCOME OF THIS PROJECT

3. The outcome of this project is an increased understanding of the details and scope of different regulatory risk assessments for manufactured nanomaterials by comparing and contrasting the conditions, assumptions, and levels of uncertainties of approaches utilised in different jurisdictions. Best practices could be identified that could be adopted by other countries.
4. This report describes:
- OECD Member countries approaches and activities regarding risk assessment and risk management of manufactured nanomaterials;
 - The different levels of uncertainties in those approaches and why these differences are present;
 - Common knowledge gaps most relevant to risk assessment and risk management approaches for manufactured nanomaterials; and

- Recommendations on how risk assessments could be improved to reduce uncertainty regarding manufactured nanomaterials.

SURVEY RESULTS

GENERAL RESPONSES

5. A survey was sent to the OECD Working Party on Manufactured Nanomaterials (WPMN) on March 29, 2016. The survey is attached as an Annex. Fourteen responses were received from WPMN member countries (Australia, Canada, Denmark, Germany, Japan, Korea, Netherlands, Switzerland, United Kingdom, and United States) and one from the Business and Industry Advisory Committee to the OECD (BIAC). All respondents were government agencies with the exception of one industry response. Most respondents conducted nanomaterial assessments either as part of their statutory obligation to assess and manage risks for chemical substances or to improve/identify data gaps/alternative assessment of chemical substances that are nanomaterials. Others were focused on assessing certain products, where the products contained nanomaterials or a specific nanomaterial.

6. A typical nanomaterial definition is based on chemicals with particles in the 1-100 nm range including other caveats or exceptions. Most respondents identified size or size distribution as the property used to identify a chemical substance as a nanomaterial. A few respondents also noted surface area or shape. Others either identified no criteria or noted that the focus was assessing risks from certain products that contained nanomaterials but the nanomaterials were not characterized.

7. When assessing nanomaterials about half of the respondents considered control technologies such as engineering controls to prevent human exposure or waste treatment to limit environmental release. The other half of the respondents did not report using control technologies or did not give a response.

8. Six respondents reported the use of exposure limit values. The limit values described below were for numerous specific nanomaterials including silver, carbon nanotubes, and titanium dioxide and a general reference value for nanomaterials. Some of the limit values are not based on data for a specific nanomaterial or a nanoform of a chemical substance.

9. In the United States the following two values are used as acceptable exposure limit values for carbon nanotubes and ultrafine (nano-sized) titanium dioxide when assessing risks under the Toxic Substances Control Act:

- National Institute of Occupational Safety and Health Recommended Exposure Limit for carbon nanotubes of $1 \mu\text{g}/\text{m}^3$. The document describing how the limit was derived is available at:

<https://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf> (US NIOSH, 2013_[2])

- National Institute of Occupational Safety and Health Recommended Exposure Limit for ultrafine (nano-sized) titanium dioxide of 0.3 mg/m³. The document describing how the limit was derived is available at:
<https://www.cdc.gov/niosh/docs/2011-160/pdfs/2011-160.pdf>. (US NIOSH, 2011_[3])
10. Canada reported using the United States Environmental Protection Agency (EPA)'s reference dose (RfD) for silver in natural health products available to consumers. Canada noted that the silver used in these products is sometimes in a nanoform. For silver, the level is 5 µg/kg/day orally (EPA RfD for silver in general). Canada noted this value can be lower on a case- by-case evaluation basis. For information on this exposure limit go to: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0099_summary.pdf (US EPA, 2003_[4])
 11. In Japan METI reported that risk assessments of three nanomaterials (Risk Assessment of Manufactured Nanomaterials – Titanium Dioxide, Risk Assessment of Manufactured Nanomaterials – Fullerene, Risk Assessment of Manufactured Nanomaterials – Carbon Nanotubes) were developed and published. The three reports on the risk assessment include occupational exposure limits and direction on risk management methods recommended by the project. They are available from: <http://en.aist-riss.jp/assessment/2721/> (AIST, 2013_[5])
 12. METI further reported using no-observed-adverse-effect level (NOAEL) values obtained from available inhalation exposure tests that were extrapolated to human values (occupational) by adjusting exposure conditions and applying uncertainty factors. The occupational exposure limit values (OELs) were proposed to support current management of the occupational environment. The OEL values were derived as period-limited values by assuming a sub-chronic exposure period of approximately 15 years on the condition that a re-evaluation be conducted within the next ten years or so. The proposed OELs (PL, period-limited) were 0.03 mg/m³ for carbon nanotubes (CNT), 0.39 mg/m³ for fullerene (C60), and 0.61 mg/m³ for titanium dioxide (TiO₂) nanomaterials. See the risk assessments for details.
 13. In the Netherlands provisional nano-reference values are used ([Dekkers et al 2010](#)), but as these are not health based the respondent noted they should be used with care. For more information go to: <http://www.rivm.nl/bibliotheek/rapporten/601044001.html> (Dekkers S, 2010_[6])
 14. In Switzerland the recommended MAK (Maximale Arbeitsplatz-Konzentration, i.e. threshold limit value) for carbon nanotubes (length >5 µm, diameter <3 µm, aspect ratio length/diameter >3:1) is set at 0.01 fibers/mL. It is the same value as the MAK for asbestos fibers.
 15. Denmark published ecotoxicological data and Predicted No-Effect Concentrations (PNECs) for nine selected nanomaterials which are considered to be environmentally relevant due to high usage volumes or how they are used. These data, together with data from other reports/projects, were used in an overall assessment of the environmental risk of nanomaterials in Denmark. The nine investigated nanomaterials are: titanium dioxide, zinc oxide, silver, carbon nanotubes, copper oxide, zero valent iron, cerium dioxide, quantum dots and carbon black. For more details, see: <http://mst.dk/service/publikationer/publikationsarkiv/2015/nov/environmental-effects-of-engineered-nanomaterials/> (Ministry of Environment and Food of Denmark, 2015_[7])

16. BIAC reported use of defined internal exposure limits for some nanomaterials.
17. Many respondents reported either requiring or identifying data to be used to assess nanomaterials that was different than the data used to assess conventional chemicals. Several of the jurisdictions reported they required a prescribed data set for all chemicals at certain production volumes, although the data was not always appropriate or useful for characterizing or assessing nanomaterials. Those jurisdictions reported taking further actions to obtain different data for nanomaterials. One example was Canada requiring different data when further reporting was required under its Significant New Activity provisions.
18. There were five respondents that did not identify using or requiring any different data to assess nanomaterials. Several of these respondents were reporting on assessing specific products that contained nanomaterials rather than a specific nanomaterial.
19. Numerous respondents did not give specific examples of different data as they stated that the types and categories of different data varied depending on the nanomaterial and other variables in the assessment. All respondents who identified using different data for assessing nanomaterials identified using different physical-chemical data. Most of them also identified using different fate, exposure, and toxicity data to assess nanomaterials.

SOME SPECIFIC EXAMPLES

20. In Japan, in the risk assessment practice in the New Energy and Industrial Technology Development (NEDO) project, different physical-chemical properties were required for carbon nanotubes. The length and width were required for fibrous nanomaterials such as carbon nanotubes while only diameter was required for spherical nanomaterials. For carbon nanomaterials such as carbon nanotubes, metal impurity information was also required.
21. In the United States these typical physical-chemical endpoints are required or recommended for specific nanomaterials:
22. For carbon nanotubes:
- Average tube diameter (inside and out)
 - Tube length and whether there is tube bending or branching
 - Number of walls and whether the walls are concentric, scrolled, or other
 - The extent of tube end-capping (closed (capped), open, or partially closed)
 - The extent of any catalyst incorporation
 - particle size of residual catalyst (if in a nanoform)
 - What percentage of surface carbons may have groups attached (if present)
 - Aggregation and/or agglomeration state
 - % residual amorphous carbon (or thermogravimetric analysis (TGA))
 - Single or double walled impurities (if any)
 - If the tube is surface modified: Surface chemistry (including elemental composition and description of surface bonding) using infra-red (IR), energy

dispersive X-ray spectrometry (EDS), electron energy loss spectroscopy (EELS), X-ray photoelectron spectroscopy (XPS), Auger electron spectroscopy (Auger), or atomic force microscopy (AFM).

- Surface area by BET (Brunauer-Emmett-Teller theory) and porosity by nitrogen (N₂) adsorption.
 - Electron microscopy (TEM/SEM) images that show the morphology of the tubes.
23. For metal oxides:
- Particle Size Distribution: 2 methods should be used; transmission electron microscopy (TEM) for dry particles and centrifugal liquid sedimentation (CLS) or dynamic light scattering (DLS) for liquid particle dispersions.
 - TEM, scanning electron microscopy (SEM), scanning transmission electron microscopy (STEM), AFM, methods for:
 - Surface area (BET)
 - Aggregation and agglomeration state
 - Morphology
 - X-ray diffraction (XRD) for the presence of any crystalline phases
 - Porosity by N₂ adsorption (if the material is assumed to be porous).
 - If applicable: Surface chemistry (including elemental composition) by EELS, XPS, EDS, Auger, or AFM.
 - If applicable: % surface coverage by ligands (applicable to quantum dots).
24. In the United States when requiring or recommending a 90-day inhalation study for carbon nanotubes the following extra requirements are identified in addition to those in OECD test guideline 413. Specific testing requirements language:
- A 90-day inhalation study by nose-only administration in male or female rats with up to a 9-month observation post exposure with bronchoalveolar lavage fluid (BALF) analysis. In addition, the following data will be submitted;
 - Evaluation includes markers of damage, oxidant stress, cell proliferation, the degree/intensity and duration of pulmonary inflammation, fibrosis, and cytotoxic effects in the bronchoalveolar lavage fluid (BALF) and histopathology of pulmonary and extra-pulmonary organs/tissues (cardiovascular, central nervous system, liver, kidney, etc.). Determine the potential for cardiovascular toxicity through monitoring of the most sensitive blood and/or plasma endpoints indicative of cardiovascular effects. Data on pulmonary deposition (lung burden), clearance half-life (biopersistence) and translocation of the test material. Differences in the physical-chemical properties of the as-administered material relative to the as-produced material shall be provided (to include size distribution information and other toxicologically relevant properties). Techniques used to produce the as-administered material shall be described. The proposed protocol for testing should be provided to EPA for review and comment prior to the initiation of testing. A minimum set of BALF parameters and size for aerosols to be administered: the minimum set of BALF measurements would consist of total protein and/or albumin, acellular lactate dehydrogenase (LDH), and cell

differentials (total cells, lymphocytes, macrophages, and polymorphonuclear leukocytes). Aerosols should be used whose particles have a Mass Median Aerodynamic Diameter (MMAD) of up to 2 µm, with a geometric standard deviation (GSD) up to 3 µm (unless human exposure data dictates a more realistic size distribution).

METHODS USED

25. Respondents noted using various tools for assessing nanomaterials such as:
- Test data on the specific substance;
 - Use of analogue data;
 - Use of models with limitations described further below; and
 - Use of published literature.
26. The challenges associated with assessing nanomaterials fell into two broad categories. There was either a lack of data, or uncertainty that available data or models were applicable to the nanomaterial. See the next section for a discussion of models.
27. For those respondents who reported using models to estimate exposures or hazards, several reported a high level of uncertainty due to limitations of the models applicability to nanomaterials, because the model was not validated for nanomaterials or it was based on conventional chemicals. Some respondents reported using existing models that have been adapted or validated for nanomaterials. Several respondents reported they did not use models to assess nanomaterials as they had not been validated for nanomaterials.
28. Respondents reported using the following models that had not been designed or adapted for nanomaterials: ChemSTEER (US EPA, 2013_[8]), EFAST (US EPA, 2014_[9]), and Consumer Exposure Model (CEM) (US EPA, 2017_[10]).
29. Respondents also reported using the following models that had been adapted for nanomaterials:
- ECETOC TRA
<http://www.ecetoc.org/tools/targeted-risk-assessment-tra/> (European Centre for Ecotoxicology and Toxicology of Chemicals,(n.d.)_[11])
 - Stoffenmanager Nano
<https://nano.stoffenmanager.nl/> (Cosanta,(n.d.)_[12])
 - Nanotool (Denmark)
<http://www2.mst.dk/udgiv/publications/2011/12/978-87-92779-11-3.pdf> (The Danish Environmental Protection Agency, 2011_[13])
 - ISO control banding approach
<http://www.safenano.org/knowledgebase/guidance/banding/iso-2014-occupational-risk-management-applied-to-engineered-nanomaterials-control-banding/> (ISO, 2014_[14])
 - French ANSES document on control banding

<https://www.anses.fr/en/system/files/AP2008sa0407RaEN.pdf> (ANSES, 2010_[15])

- Precautionary Matrix for Synthetic Nanomaterials
<https://www.bag.admin.ch/bag/en/home/themen/mensch-gesundheit/chemikalien/nanotechnologie/sicherer-umgang-mit-nanomaterialien/vorsorgeraster-nanomaterialien-downloadversion.html> (Federal Office of Public Health of Switzerland, 2016_[16])
- ConsExpo nano (inhalation exposure from consumer products),
<https://www.consexponano.nl/> (The Dutch National Institute for Public Health and the Environment (RIVM), 2016_[17])
- SimpleBox for nano (environmental fate).
http://www.rivm.nl/en/Topics/S/Soil_and_water/SimpleBox (RIVM, 2014_[18])
- NanoDUFLOW has been used at smaller scales (e.g. catchment) for environmental exposure assessment.
<https://www.sciencedirect.com/science/article/pii/S0043135415300099> (Quik, de Klein and Koelmans, 2015_[19])

30. The US EPA reported using its chemical category of poorly respirable soluble particles category to assess hazards of certain nanomaterials such as carbon nanomaterials, metals, and metal oxides. For a description of this category and its parameters, see: https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf (US EPA, 2010_[20])

31. Regarding the validity of test methods most respondents reported using a weight of evidence approach to validate test results from available scientific methods for nanoscale and non-nanoscale forms of chemicals. These generally involve comparing the characterization of the chemicals being tested and the nanomaterials being assessed. Many respondents noted this led to approaches that were used and applicable on a case-by-case basis and in many cases involved expert judgment. Most respondents also reported using available OECD test methods.

SOME SPECIFIC EXAMPLES DESCRIBED

32. Intratracheal administration tests which are often available in peer-reviewed literature were used to estimate hazard. Subacute inhalation toxicity tests were also used. Careful sample preparation and characterization of test samples (aerosol for inhalation tests and dispersion for intratracheal administration) are important for evaluating such studies. The effect of sample preparation conditions on the test results might be one of the uncertainties.

33. For the derivation of a PNEC of nanosilver NM-300 K in soil upon application of nanosilver treated sludge, a combination of the OECD TG 216 and the ISO method for determining the potential nitrification and inhibition of nitrification (ISO 15685) was used. This ISO method is used to investigate the ammonium oxidation in soils containing a population of nitrifying microorganisms. This adaptation of the test execution was necessary since the application of sludge to the soils raised the content of nitrate significantly. Due to this high background of nitrate it would not be possible to detect the additional nitrate accumulation during the incubation period. By measuring the potential

ammonium oxidation according to the ISO method, it was possible to avoid the interfering effect of the added nitrate as well as to potentially identify effects on the second process of nitrification.

ADAPTATIONS AND IDENTIFIED NEEDS FOR ADAPTATIONS (FROM CONVENTIONAL CHEMICALS)

34. Most respondents reported adopting approaches for assessing conventional chemicals to assess nanomaterials. Some reported using data for a non-nanoscale version of a nanomaterial to assess physical properties and hazard. Others reported applying the same approaches or models used for conventional chemicals to assess hazard, exposures, fate, and physical properties. Some respondents identified environmental exposures as something they did not adapt from conventional chemicals because the validation was lacking or uncertainty was too great. Many of the models noted, in #24 of Section 2.3 Methods Used, are adapted from or for assessments of conventional chemicals. Several respondents used the phrase or a phrase meaning “extended characterization requirements” to describe using the same methods for assessing conventional chemicals but utilizing additional physical-chemical properties for nanomaterials.

35. In several cases respondents noted using worst case exposures or bounding estimates to assess worker exposure and environmental releases. These bounding estimates were used instead of estimates based on modeling or data for similar non-nanoscale chemicals. For example, estimates of exposure of wastewater treatment plant operatives would be based on no removal from waste water treatment and also 100% partitioning to biosolids after complete removal from wastewater treatment.

SOME SPECIFIC EXAMPLES IDENTIFIED:

Occupational Exposure Assessment and Limits

36. In Switzerland there is no general specific limit value for nanomaterials although there is one for carbon nanotubes as noted in #12 of Section 2.1 General Responses of this report. There is a general MAK-value of 3 mg/m³ for respirable inert dust and a recommended value for sensitizing dust of 2 mg/m³ over 15 minutes of exposure.

37. In the United States there is an Occupational Safety Health Administration (OSHA) dust standard limit of 15 mg/m³ for respirable particles: https://www.osha.gov/dts/chemicalsampling/data/CH_259635.html (US OSHA, 2012_[21])

38. There are also reference documents from the United States EPA for release and exposure assessment, inhalation monitoring, engineering controls and use of personal protective equipment: https://www.epa.gov/sites/production/files/2015-09/documents/cebnanodraft_05_12.pdf (US EPA, 2012_[22])

39. In Japan, in the risk assessment practice in the NEDO project, to derive occupational exposure limits, the NOAEL values obtained from *in vivo* tests were extrapolated to human exposures (occupational) by adjusting exposure conditions and applying uncertainty factors. This could be regarded as a model for extrapolation. In the C60 exposure assessment in the occupational environment, near-field and far-field model (a kind of 2-box model) was used to predict the exposure concentration during handling of the material. Although they have not been validated for nanomaterials, the factors specific to the nanomaterials were taken into account. For example, deposition rates in the lung after inhalation were set based on the characterization of the aerosol.

Environmental Exposures

40. In Germany, for the case study on nanosilver NM-300K, different assumptions were used in order to derive release rates for nanosilver from textiles during washing, e.g. the fraction of nanosilver in textiles released per wash. A conservative estimate was used for a worst case approach. To account for the uncertainties in the exposure estimation, low, moderate and high environmental release of nanosilver from textiles used for domestic purposes were considered using data from washing experiments with different types of furnishings and fibers, which led to low, moderate and high release rates.

41. The United States EPA identified reference documents for exposure bounding estimates it uses to assess nanoscale materials. For environmental exposures: <https://www.epa.gov/sites/production/files/2015-09/documents/nanomaterial.pdf> (US EPA, 2010_[23])

42. Adsorption coefficients had to be used in the German case study to deduce PECs (predicted environmental concentrations) for nanosilver NM-300K for soil and sediment. However, the underlying assumptions of these coefficients were identified as inappropriate for nanomaterials. For the calculation of environmental concentrations of traditional chemicals in soil and sediment Freundlich equations are deployed. However, the suitability of these kinds of coefficients in order to describe the distribution of nanomaterials between certain phases is highly debated (e.g. in (Praetorius et al., 2014_[24])).

Hazard Assessment

43. Also in the German case study on nanosilver NM-300K, for the derivation of PNECs for nanosilver NM-300K several assumptions had to be made, which are usually applied for the effect assessment of conventional chemicals. They were identified as inappropriate as they might misguide the assessment of nanomaterials. The interpretation of ecotoxicological effect values of nanomaterials is quite challenging since these values are influenced by many factors, e.g. agglomeration behaviour and ion release rate which change bioavailability. Nominal concentrations were applied for the PNEC calculation. It can be assumed that PNECs for the aquatic compartment are lower if they are drawn upon concentrations measured in the water phase.

44. As previously reported in #24 of Section 2.3 Methods Used, the United States EPA reported using its chemical category of poorly respirable soluble particles category to assess hazards of certain nanomaterials such as carbon nanomaterials, metals, and metal oxides. For a description of this category and its parameters, see: https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf (US EPA, 2010_[20])

DATA GAPS

45. Most respondents reported:

- Validation of release/exposure scenarios for nanomaterials as one of the most important data gaps;
- Lack of agreement on standard physical-chemical properties to be measured when:
 - Preparing nanomaterial samples for testing;

- Characterizing nanomaterials being assessed; and
 - Predicting environmental fate or hazards
46. Some respondents reported:
- That the concepts of grouping and read-across on all aspects of risk assessment of nanomaterials are not reliable and need to be developed;
 - There is a need for validated OECD test guidelines for nanomaterials.

LESSONS LEARNED / BEST PRACTICES

47. Other suggestions in terms of additional key needs include:
- Develop uncertainty factors specific to nanomaterials for hazard assessments;
 - Develop and validate adverse outcome pathways (AOPs) for nanomaterials;
 - Identify and agree to a minimum set of parameters for assessing different types of nanomaterials;
 - Develop more information on specific aspects of hazard assessment for nanomaterials:
 - Hazards of nanomaterials in articles;
 - Chronic exposure to nanomaterials;
 - Extrapolation of *in vivo* test results to humans; and
 - Development of screening tests or tiered testing approach.
48. Examples of known hazards associated with nanomaterials:
- Based on receipt of multiple 90-day inhalation studies carbon nanotubes cause lung effects at very low doses due to the presence of respirable particles.
49. While no clear best practice emerged, some suggested approaches include:
- Consider the physical forms of nanomaterials when assessing and limiting risk as some forms will have greater risk than others;
 - Assume nanomaterials are more mobile (may disperse further) or become more easily aerosolized than non-nanoscale materials to account for greater uncertainty;
 - Focus on safe use in particular products rather than identify uses with potential risks;
 - Current risk assessments require limited adaptation for first generation nanomaterials, but this may be greater as second and third generation nanomaterials are developed. It was suggested that a list of potential issues/features be identified in order to undertake analysis of whether these present challenges for the existing models/methods.

RECOMMENDATIONS

50. Below is a list of recommendations identified by a majority of survey participants:

- There is further need for validated exposure/release scenarios and assessment for nanomaterials;
- The utility of specific physical-chemical properties to predict environmental fate and hazard must be validated in order to agree a set of required characterization parameters, which will likely be specific to the type of nanomaterial being assessed;
- It is essential to improve the ability to use read-across/grouping/screening tests to assess nanomaterials; and
- There needs to be continued development of validated test guidelines specific to nanomaterials.

CONCLUSIONS

51. The results of the survey provided two general outcomes. The first is that there is general agreement by survey respondents on the most relevant data gaps and future activities that should be addressed to improve the risk assessment of nanomaterials. The other is that survey respondents identified numerous specific examples of using available tools to assess nanomaterials even when faced with continued uncertainty of the hazards.

52. There is a wide variety of approaches of tools used to assess and manage risks of nanomaterials. Some of the approaches are specific to nanomaterials but many are based on adaptations of approaches for conventional chemicals. Regardless of the approach used the level of uncertainty remains high.

53. Everyone will not agree on each approach used and several respondents identified additional data gaps and future activities for consideration. The responses do identify issues for further consideration and possible adaptation. It should be noted that all the data gaps identified by a majority of respondents and even some of those identified by only fewer respondents are already being addressed by OECD's WPMN projects.

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ANNEX - SURVEY

OECD WPMN SURVEY ON THE TYPES OF REGULATORY RISK ASSESSMENTS OF MANUFACTURED NANOMATERIALS IN OECD COUNTRIES

The purpose of the survey is to investigate different types of assessments used to inform risk assessment outcomes and risk management measures of different jurisdictions. By comparing and contrasting the conditions, assumptions, and levels of uncertainties of these risk assessments of manufactured nanomaterials, best practices could be identified that could be adopted by other countries.

Introductory Questions

1. Have you evaluated any nanomaterials? Yes No
 - a. If the answer is no then you do not need to respond to the survey.
 - b. If the answer is yes then which properties did you use to identify the chemical substance as a nanomaterial?
 - Size
 - Size distribution
 - Surface Area
 - Other – Please describe

Methods and processes for risk assessment of nanomaterials

2. What is the purpose of your risk assessment? E.g., a screening-level assessment, qualitative control banding, or a quantitative risk determination?
3. What are the possible outcomes? (risk management measures, data generation, or other outcomes)
4. What tools have been used to assess risks? For example use of analogue data or exposure estimates based on modeling.
Are there any challenges associated with applying these measures to nanomaterials?

5. How do your legal/regulatory requirements affect your assessment and your risk management of nanomaterials? E.g., do the regulations set standards for risk/hazard or do they require certain test data?

6. Do you take control technologies or risk reducing methods into account during the risk assessment such as engineering controls to prevent exposure or waste treatment to limit release? Yes No

Do you have pragmatic or temporary limit values for exposure to certain nanomaterials? For example in the United States the National Institute of Occupational Safety and Health has a recommended exposure limit for carbon nanotubes.

Yes No

If you answered yes please identify any methods or values used.

Uncertainties, data requirements, and characterization/identification parameters used

7. Do you require different data to evaluate different nanomaterials?

For example are data required for carbon nanotubes different than for metal nanoparticles? Are different data required for gold and silver nanoparticles?

Yes No

If yes does this apply to physical-chemical properties

fate

exposure

toxicity data

8. In the absence of nano-validated OECD test methods, how are you considering validity of test methods to support nanomaterial risk assessments?

9. Are you actively using test methods published by other organizations (e.g., ISO or OECD) or in peer-reviewed literature?

Yes No

If yes please identify any adaptations that have been required or uncertainties that are being applied to account for nanomaterials?

10. Are there any nano-specific knowledge gaps in risk assessments such as hazard assessment, exposure assessment, or environmental assessment?

Yes No

If yes, what are they?

Adaptation of approaches from conventional chemicals

11. Are approaches used for the risk assessment of nanomaterials currently being used based on conventional chemicals? Yes No

If yes:

- a. What adaptations are being made to make these approaches relevant for nanomaterials?
- b. Do you use different assumptions? Identify any uncertainties that are being applied?
- c. Are any models you use to estimate exposure or hazard applicable? Yes No

If yes have they been validated for nanomaterials?

Additional suggestions on how to improve risk assessment for nanomaterials

12. Are there any methods, best practices, or lessons learned that have been applied in your jurisdiction to reduce uncertainties or improve risk assessment methodologies that could be shared?

13. What is the knowledge gap or lesson learned that could most improve risk assessments?