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Developing a Guidance Document for the testing of dissolution and dispersion stability of nanomaterials, and the use of the data for further environmental testing and assessment strategies

Final report

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Developing a Guidance Document for the testing of dissolution and dispersion stability of nanomaterials, and the use of the data for further environmental testing and assessment strategies

Final report

by

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Abstract: Developing a Guidance Document for the testing of dissolution and dispersion stability of nanomaterials, and the use of the data for further environmental testing and assessment strategies

In this report the background, course and content of the development of an OECD Guidance Document (GD) for the testing of dissolution and dispersion stability of nanomaterials in the environment and the use of data on these endpoints for further environmental testing and assessment strategies is presented.

The dissolution (rate) and dispersion stability of nanomaterials are considered as main drivers determining environmental fate and behavior in the environment. There is already an OECD Test Guideline (TG) 318 on dispersion stability of nanomaterials in the environment, and an OECD TG on dissolution (rate) of nanomaterials in the environment is still under development.

As no specific OECD TG for dissolution for nanomaterials is available, the GD integrates methods meaningful for nanomaterials present from science or available by OECD TG/GDs. Also regards to TG318 for dispersion stability, more information on data presentation and interpretation is added to the GD. Furthermore, important interim guidance on testing heteroagglomeration of nanomaterials in the environment is given.

The report also presents the importance of this GD for environmental assessment of nanomaterials as well as gives an insight into the regulatory implications it may have in future.

The final GD was adopted by OECD Working Group of National Co-ordinators of the OECD Test Guidelines Programme (WNT) in April 2020 and can be found at the webpages of the OECD Test Guideline Programme upon publication.

Kurzbeschreibung: Entwicklung eines Leitfadens zur Untersuchung von Löslichkeit und Dispersionsstabilität von Nanomaterialien und die Nutzung der gewonnen Daten für weitere Umweltuntersuchungen und - Bewertungsstrategien

Dieser Bericht präsentiert den Hintergrund, Ablauf und die Inhalte zur Entwicklung eines OECD Leitfadens für die Untersuchung von Löslichkeit und Dispersionsstabilität von Nanomaterialien in der Umwelt und die Nutzung der dadurch gewonnenen Daten für weitere Umweltuntersuchungen und Umweltbewertungsstrategien.

Die Löslichkeit(srate) und Dispersionsstabilität werden als die wichtigsten Treiber des Umweltverhaltens und –schicksals von Nanomaterialien in der Umwelt angesehen. Zur Bestimmung der Dispersionsstabilität von Nanomaterialien in der Umwelt liegt bereits die OECD Prüfrichtlinie (TG) 318 vor. Eine OECD Prüfrichtlinie zur Bestimmung der Löslichkeit(srate) von Nanomaterialien in der Umwelt befindet sich derzeit noch in der Entwicklung.

Da noch keine solche OECD Prüfrichtlinie zur Bestimmung der Löslichkeit(-rate) für Nanomaterialien zur Verfügung steht, wurden in den Leitfaden solche Methoden aus Wissenschaft und vorliegenden OECD TG/GDs aufgenommen, die für Nanomaterialien als sinnvoll erachtet werden. Zur Unterstützung der Anwendung der OECD TG 318 sind zusätzliche Informationen zur Präsentation und Interpretation von Daten zur Dispersionsstabilität in den Leitfaden eingebracht worden. Darüber hinaus werden im Leitfaden vorläufige Anleitungen gegeben, wie Heteroagglomeration von Nanomaterialien in der Umwelt bestimmt werden kann.

Der vorliegende Bericht stellt neben den Inhalten des Leitfadens und den Ablauf seiner Entwicklung auch seine Bedeutung für die Umweltbewertung von Nanomaterialien dar und gibt einen Ausblick, welche regulatorischen Tragweite dieser in der Zukunft haben kann.

Der finale Leitfaden wurde im April 2020 von der OECD Arbeitsgruppe der Nationalen Koordinatoren des OECD Prüfrichtlinienprogramms (WNT) verabschiedet und ist nach Veröffentlichung auf den Internetseiten des OECD Prüfrichtlinienprogramms zu finden.

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Agglomeration – Process of contact and adhesion whereby dispersed particles are held together by weak physical interactions ultimately leading to enhanced sedimentation by the formation of particles (agglomerates) of larger than colloidal size. In contrast to aggregation where particles held by strong bonds like sinter bridges, agglomeration is a reversible process.

Dissolution – Process under which a substance is dissolving.

Dissolution rate – The amount of substance dissolved (solute) into a solvent over time.

Heteroagglomeration – Agglomeration of particles (here nanomaterials) with other particles (synthetic or natural).

Homoagglomeration – Agglomeration of particles (here nanomaterials) with the same nanomaterial.

NOM – Natural organic matter: the organic substances present in surface or ground water. NOM covers humic and non-humic fractions as e.g. polysaccharides. NOM is operationally divided into Dissolved Organic Matter (DOM) and Particulate Organic Matter (POM). DOM passes a 0.45 µm filter, POM is retained by the same filter. POM as defined herein should not be confused with purgeable organic carbon.

Size – Size of the particles, aggregates or agglomerates is given in micrometres (µm) or nanometres (nm). Particle size usually refers to the particle size distribution. The method for particle size determination and relevant parameters of the particle size average should be reported.

Solubility - The quantity of solute that dissolves in a given quantity of solvent to form a saturated solution.).

SRNOM – Suwannee River NOM: a standard surface water NOM material of the International Humic Substance Society (IHSS), isolated from the Suwannee River (US) by reverse osmosis and purified according to the procedures of the IHSS. The material can be purchased from the IHSS.

WNT - Working Group of National Co-ordinators of the OECD Test Guidelines Programme at OECD

WPMN - Working Party on Manufactured Nanomaterials at OECD

Summary

This report presents background, course and content of the development of an OECD Guidance Document (GD) for the testing of dissolution and dispersion stability of nanomaterials in the environment and the use of data on these endpoints for further environmental testing and assessment strategies.

Both endpoints - dissolution (rate) and dispersion stability of nanomaterials - are considered as main parameters determining environmental fate and behavior in the environment. As such, clear guidance is needed for collecting data on these parameters with improved reliability, repeatability and robustness.

While there already is an OECD Test Guideline on dispersion stability of nanomaterials in the environment (TG 318, OECD 2017), an OECD Test Guideline on dissolution (rate) of nanomaterials in the environment is still pending.

The GD was included in the Work Plan of the Working Group of National Co-ordinators of the OECD Test Guidelines Programme (WNT) in 2014 as project 3.9 lead by Germany together with the project on developing TG 318 and the intended TG on dissolution (rate) of nanomaterials in the environment (WNT project 3.10). The GD presented in this report was developed from 2017 until 2020, with preliminary work started in 2013. Two national research projects were dealing with the development of this GD, while the second project is presented in this report. The GD was developed with the support of a number of scientists with strong expertise in the field and the support of OECD secretariat and delegations of OECD Working Party on Manufactured Nanomaterials (WPMN) and national experts of the OECD WNT. The final GD was adopted by OECD WNT in April 2020 and can be found at the webpages of the OECD Test Guideline Programme upon publication.

Next to an overview of the development of the GD, the report describes the contents of the final GD, gives a rationale for their inclusion and highlights the importance of this GD for environmental assessment of nanomaterials as well as gives an insight into the regulatory implications it may have in future.

Zusammenfassung

Dieser Bericht präsentiert den Hintergrund, Ablauf und die Inhalte zur Entwicklung eines OECD Leitfadens für die Untersuchung von Löslichkeit und Dispersionsstabilität von Nanomaterialien in der Umwelt und die Nutzung der dadurch gewonnenen Daten für weitere Umweltuntersuchungen und Umweltbewertungsstrategien.

Beide Endpunkte - Löslichkeit(srate) und Dispersionsstabilität - werden als wichtigste Parameter zur Bestimmung des Umweltverhaltens und –schicksals von Nanomaterialien in der Umwelt angesehen. Aus diesem Grund sind eindeutige Anleitungen notwendig, wie Daten zu diesen Parametern für eine verbesserte Verlässlichkeit, Reproduzierbarkeit und Belastbarkeit erhoben werden sollten.

Während für die Bestimmung der Dispersionstabilität von Nanomaterialien in der Umwelt bereits eine OECD Prüfrichtlinie besteht (TG 318, OECD 2017), fehlt es derzeit noch an einer OECD Test Prüfrichtlinie zur Bestimmung der Löslichkeit(srate) von Nanomaterialien in der Umwelt.

Die Arbeiten zur Entwicklung dieses Leitfadens wurden von Deutschland koordiniert und 2014 als Projekt 3.9 in den Arbeitsplan der Arbeitsgruppe der Nationalen Koordinatoren des OECD Prüfrichtlinienprogramms (WNT) zusammen mit dem Projekt zur Entwicklung der TG 318 und dem Projekt für eine TG zur Bestimmung der Löslichkeits(rate) (WNT Projekt 3.1) aufgenommen. Der Leitfaden, der in diesem Bericht vorgestellt wird, wurde von 2017 bis 2020 entwickelt. Vorarbeiten dazu erfolgten bereits ab 2013. Zwei nationale Forschungsvorhaben beschäftigten sich mit der Entwicklung dieses Leitfadens, wobei das zweite dieser Projekte in diesem Bericht vorgestellt wird.

Der Leitfaden wurde mit Unterstützung einer Gruppe von Wissenschaftlern mit großer Expertise in den entsprechenden Bereichen sowie mit der Hilfe des OECD Sekretariats und Delegationen der OECD Working Party on Manufactured Nanomaterials (WPMN) und nationalen Experten der OECD WNT entwickelt. Der finale Leitfaden wurde im April 2020 von der OECD WNT verabschiedet und ist nach Veröffentlichung auf den Internetseiten des OECD Prüfrichtlinienprogramms zu finden.

Neben dem Überblick über die Entwicklung des Leitfadens beschreibt der Bericht auch die Inhalte der finalen Version des Leitfadens und begründet aus wissenschaftlicher Sicht warum diese Eingang in den Leitfaden gefunden haben. Er stellt die Relevanz des Leitfades für die Umweltbewertung von Nanomaterialien dar und gibt einen Ausblick zu seiner möglichen regulatorischen Bedeutung.

1 Introduction

At the OECD Expert Meeting in Berlin 2013 (OECD 2014a), it was discussed and then identified that dissolution rate and dispersion stability in the environment are important parameters for nanomaterials. Hence, these parameters are main drivers in environmental fate of nanomaterials and nanomaterial`s including their (bio)availability, and as such important in environmental risk assessment of nanomaterials. At the time it was concluded that Test Guidelines (TGs) should be developed for these parameters. As these two features (dissolution and dispersion stability) are often interlinked it was noted that an overarching guidance document (GD) would be useful to explain e.g. the pitfalls of the methods, interaction between dissolution and dispersion stability, and to give broader understanding to all available methods and for the interpretation of the results gained with these methods.

The first draft of Guidance Document (GD) was developed within the course of the development of the TG 318 on dispersion stability (OECD 2017) (Kozin and von der Kammer, 2017). Based on this draft, the development of the GD was continued within a research project which outcomes are presented here. This report describes the objectives, organization, course and content of GD as well as outlines the relevance for environmental risk assessment.

The guidance collected in the GD and presented in this report is relevant for solids in nanoscale as well as their aggregates and agglomerates. It follows the definition of nanomaterials as having one dimension between 1 and 100 nm. The GD aims to serve as a support tool for both the TGs, to provide guidance on the influence of various experimental conditions and materials on the performance and outcomes of the TGs, as well to advice on modifications and additions based on specific research questions and gives support for the expression and interpretation of results.

The final version of the GD was adopted by OECD Working Group of National Co-ordinators of the OECD Test Guidelines Programme (WNT) in April 2020 and can be found at the webpage of the OECD WNT when available.

2 Development of the OECD Guidance Document

2.1 Background of the GD development

Dissolution of ions from metal, metal oxides or other metal containing nanomaterials is very important for the estimation of their environmental fate and hence also the exposure of the organisms in the environment. Either the exposure to the dissolved ions, the nano(materials) themselves or both may cause the risks to the ecosystem. Similar aspects might be also relevant for organic nanomaterial that can solve in aqueous media.

Dispersion stability in various environmental conditions commands where the nanomaterial in question goes to. Dispersion stability determines whether the nanomaterial is quickly sedimented in an aquatic environment or whether it stays in the water column as dispersion. Depending on this parameter different scenarios for the risk assessment are anticipated and different organisms are affected by nanomaterial exposure (either mostly benthic organisms in/at the sediment or those pelagic ones in the water column).

For a reliable, robust and repeatable determination of dissolution and dispersion stability of nanomaterials, standardised TGs are needed, as well as a guidance document (GD) to assist the (joint) use of these methods.

A TG on dispersion stability of manufactured nanomaterials in simulated environmental media is available since 2017 (TG 318, OECD 2017). In this method the (homo)agglomeration and subsequent sedimentation of nanomaterials is tested in various environmental conditions. These conditions are various pH, ion content and different concentrations of natural organic matter (NOM). Usually the “standard” NOM used is Suwannee River NOM (SRNOM), but also well characterized natural NOM can be used.

Open issues, not addressed in the TG 318 include the determination of heteroagglomeration of nanomaterials with other (natural occurring) particles. The use of such data to calculate attachment coefficient would be expedient but is not captured by the TG. Furthermore, the TG does not include support how to visualize results. Thus, to close these gaps, these issues were addressed in the GD.

The development of a TG on dissolution rate in environmental media was included as OECD WNT (Working Group of National Co-ordinators of the OECD Test Guidelines Programme) project 3.10 in the WNT work plan in 2014 (OECD 2019). The purpose of this project is to develop and adequately validate a robust method for dissolution (rate) of nanomaterials in environmental relevant media. The draft TG is still under development. Other relevant methods for dissolution rate testing in water and biological fluids (WNT project 1.5) as well as transformation in the environment (WNT project 3.16) were included in the WNT work plan.

Due to the current lack of a harmonised and validated method on dissolution rate at OECD level to be used in environmental risk assessment, it was concluded for the meantime to focus guidance on determination of dissolution and dissolution rate on all available information on static batch and dynamic flow through methods in this overarching GD, considering the efforts made for the current draft documents of WNT project 3.10, information from scientific literature, and guidance given in OECD GD 29 (OECD 2001). Once the above mentioned OECD projects are finalised and TG for dissolution testing is available, an update of the GD might be considered.

Next to the above mentioned WNT projects on TGs and GDs specific for nanomaterials, a draft GD on aquatic (and sediment) toxicity testing of nanomaterials (WNT project 2.51) was developed and adopted by WNT in parallel to the GD presented here. An additional project relevant for the work on this GD or vice versa is the draft GD on the apparent accumulation potential for nanomaterials (WNT project 3.12) as dispersion stability and ion dissolution will affect bioaccumulation testing and thus, need to be considered in a bioaccumulation testing strategy. Furthermore, guidance of this GD will become relevant for soil column testing of nanomaterials for which a GD supporting OECD TG 312 (OECD 2004) is also underway at WNT level (WNT project 3.14).

2.2 Organization and course of the GD development

The intention of the presented research project for the development of the GD for the testing of dissolution and dispersion stability of nanomaterials was to collect relevant data based on available scientific finding and expert opinion and to translate them into recommendations within the GD. For this, experts involved in the above mentioned activities and additional renowned expert in the field were invited to volunteer in a project associated expert group. From this group, a core group supporting the GD development by drafting text was established. The members of both the project associated expert group and the core group for drafting are listed in Annex 1. Several new volunteers have been interested to contribute to the GD, and the list was evolved during the project.

In a first step, a backbone of the possible contents was developed and discussed with the experts. Then the project manager developed the first drafts and these versions were commented and discussed among the experts in several meetings, teleconferences and commenting rounds. The detailed steps of the GD development are presented in Annex 2. In February 2019, a milestone of GD development was achieved. Selected members of the core group were invited to a 2-day drafting meeting for simultaneous discussion and text development of all chapters of the draft GD. Based on this meeting, in April 2019, a mature version of the draft GD was submitted for the commenting among nominated OECD WNT experts for nanomaterial environmental fate.

The comments by the WNT experts were compiled, and a new version was developed based on these comments by the contractor, and selected members of the drafting meeting. In July 2019, an accompanying Excel based spreadsheet tool was finalized by the key expert van der Kammer to be included aside to the GD. With this tool results of the TG 318 can be tabulated and utilized for data presentation.

This draft was introduced for the first commenting to the WNT with a deadline of 19th September 2019. Altogether 188 comments on the GD and the Excel tool were received from Chile, Germany, Netherlands, Sweden, United Kingdom, United States and ECHA. These were compiled, responses to the comments were developed and the GD was revised for the 2nd WNT commenting. There were still some outstanding comments on certain scientific issues which were solved with the expert advice of selected members of the core expert group and in cooperation with experts who had commented.

Starting from End of December 2019 until start of February 2020, the 2nd WNT commenting took place. Altogether ~250 comments were received from Canada, EC (JRC, ECHA), Germany, Netherlands, US, UK and BIAC. The most comments were editorial proposals to the text.

The draft GD was revised taking into account WNT comments of the 2nd commenting round. In March 2020, it was submitted for the successful GD adoption at the April 2020 WNT 32 meeting. The GD can be found freely at OECD webpages (www. oecd.org) when published.

2.3 Meetings organized for the project

Kick-of meeting

This first meeting was organized in Berlin 25th July 2017. The purpose was to fine tune the project plan and review the starting situation and the aims of the project. The notes are available from the consultant.

Stakeholder meeting

In relation to different TG and GD activities UBA organized a stakeholders meeting in Dessau 10-11th October 2017 in order to have good scientific basis for the further OECD TG and GD development. The development of the GD of this project was discussed and new experts were engaged to support this.

OECD Webex meeting of the core expert group

The (expanded) core group had a Webex meeting 11th Oct 2017 back to back to the above mentioned stakeholder meeting. The purpose of the meeting was to approve the structure of the GD and activate more experts to the core group.

Expanded core group meeting at OECD

The core group face to face meeting with additional experts with Webex possibility was organized 12 February 2018 in Paris at OECD Headquarters to inform interested experts on the project planning and current status of the GD.

Stakeholder meeting on harmonized development of OECD TGs and GDs for nanomaterials behaviour and fate

This meeting was held at the German Environment Agency in Dessau-Roßlau, 23rd-24th August 2018. Aim of this core expert meeting was to technically discuss synergies and overlaps for the ongoing and planned TG/GDs development on solubility and dissolution, dispersion stability and transformation in the environment and to promote harmonisation of these activities by enhanced cooperation and communication.

At the meeting, it was also decided to include heteroagglomeration to the GD to account for the demands of experts to also address dispersion stability under conditions affording more environmental realism. Also, issues related to the calculations and estimation of attachment efficiency should be part of the GD.

The status of the validation of the dissolution batch test as major part pf the draft TG for dissolution was presented. The draft TG was to be validated with nanoscale CuO by a rather limited number of labs. It was discussed how many nanomaterials need to be tested and in how many labs. However, it was noted that the resources for the validation exercise are very scarce. There were also several open questions regarding content and performance of the described dissolution test. It was decided that as an interim solution guidance on dissolution (rate) both in batch and dynamic flow through testing should be added to the GD.

OECD/EU WNT meeting of the joint WNT/WPNM expert groups on environmental fate and ecotoxicity of nanomaterials

The main experts involved in OECD TG and GD development for environmental fate and ecotoxicology of nanomaterials met in Arona, Italy 12-13th December 2018. The preliminary draft GD for dissolution and dispersion stability was developed by the contractor and this version was discussed. The comments from the participants were harvested during the meeting and the GD was revised again. It was also decided to organize a drafting meeting with a limited number of key experts of the core group and the contractor in late February 2019.

Drafting meeting in Berlin and further Dropbox work

The drafting meeting or writing session was organized in Berlin 27-28th February 2019. At this meeting the key experts worked on-line on various parts of the document using Dropbox facility, where also relevant literature and background material could be harvested. At the meeting a new revised draft of the GD was successfully developed, which was then edited and reorganized by the contractor for further commenting by core group and the project associated expert group, then provided to WNT for the WNT expert group commenting.

2.4 Elements of the GD

The GD aims to give advice on the two important parameters mainly triggering environmental fate of nanomaterials, which are dissolution (rate and solubility) and dispersion stability.

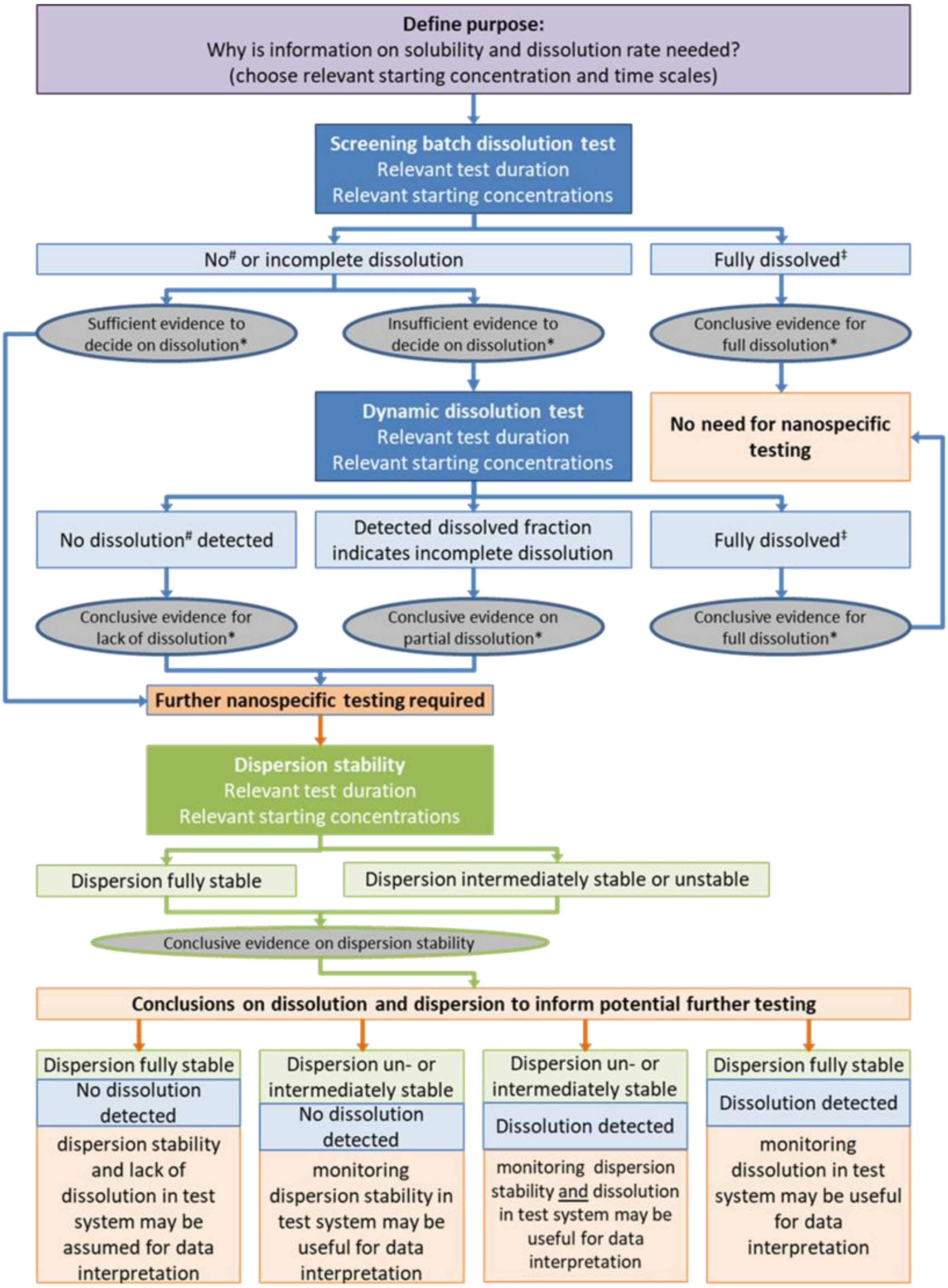
As a TG on dissolution (rate) of nanomaterials in the environment is still pending, interim guidance is given in the GD. This guidance is based on the existing draft TG (WNT project 3.10) and all available methods from OECD activities and scientific literature. It presents methods based on static batch tests to determine solubility and dissolution as well as based on dynamic methods to determine dissolution rates. It furthermore gives distinct advice under consideration of guidance given in GD 29 (OECD 2001, Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media). Finally, the GD advices how to evaluate data and which elements of testing should be reported.

As support of the existing TG 318 on dispersion stability of nanomaterials in environmental media, additional recommendations for presentation and evaluation of data are presented in the GD. An Excel tool is accompanying the GD to support visualisation of test results. Furthermore, the GD advices on alternative test conditions based on specific research questions. A major part of the GD are the recommendations on how to determine heteroagglomeration of nanomaterials which could not be addressed in the parent TG as a testing protocol for heteroagglomeration is hard to be validated based on the heterogeneity of natural suspended matter (also particles). In addition to that, equations are presented to derive attachment efficiencies of nanomaterials based on heteroagglomeration. The recommendation made on both heteroagglomeration and attachment efficiency are based on new experimental data and scientific literature.

The use of data generated by dissolution and dispersion stability testing for possible further nano-specific fate and effect testing and assessment is presented in an additional chapter of the GD. A possible testing strategy is presented which indicates decision making based on the purpose of testing and includes both batch and dynamic dissolution testing as well as dispersion stability testing based on TG 318. Depending on the outcome of these tests, the test strategy indicates important issues to be considered for data interpretation.

As such, the selection of the appropriate protocol needs to be chosen based on the purpose and objective of testing. Hence, the testing strategy and test conditions to choose are determined by whether the data is needed as basic data on environmental behaviour, to guide (eco)toxicity testing, or as input data for modelling of environmental fate. It needs to be highlighted that the GD is not intended to predict or directly correlate environmental hazard based on/with data on dissolution to derive conclusions on the relevance of the remaining nano-fraction of metal and metal oxide nanomaterials with known toxic ion release for hazard assessment. It rather offers guidance to determine essential information on the endpoints solubility and dissolution rate of nanomaterials under environmental conditions to be able to derive conclusion on their respective environmental fate to be used in exposure assessment. However, naturally, these data can also be used to support the interpretation of ecotoxicity results determined in independent tests. The proposed testing strategy of GD is presented in the Figure 1 below.

Figure 1: Overview of a testing strategy building on dissolution and dispersion stability data. # Potential dissolved fraction is below detection limit; ‡ All relevant mass of the investigated nanomaterial is in the dissolved fraction; and * The evidence takes into account relevant time scales into account.



Source: OECD Guidance Document for the testing of dissolution and dispersion stability of nanomaterials, and the use of the data for further environmental testing and assessment strategies, OECD 2020

In addition to the test strategy, the GD highlights different important issues to be considered when applying information on dispersion stability and dissolution for potential further testing.

These issues e.g. include implications connected to use of alternative test conditions, e.g. alternative test media for ecotoxicity testing and the interpretation of data for decisions on hazard testing. Furthermore, consideration on the influence of the two endpoints to each other are discussed, as. dispersion stability will influence dissolution rate and *vice versa.*

The GD also provides recommendations on the use of data from dissolution rate and dispersion stability tests according the testing strategy to derive input parameters for exposure models. These models are useful to calculate and estimate environmental fate of nanomaterials.

In a final chapter of the GD relevant links to other OECD TG and GD documents and ongoing WNT projects for nanomaterials are discussed. These include the adopted new GD on aquatic and sediment toxicity testing of nanomaterials and the foreseen GD on the apparent accumulation potential of nanomaterials in fish (WNT project 3.12). The fate testing of nanomaterials in soil is difficult to conduct and understand. Hence, the GD also gives advice on screening possibilities for dispersion stability and dissolution rates in soils, which is linked to an on-going GD development (WNT project 3.14) to support the testing of nanomaterials behaviour in soils according to OECD TG 312.

3 Relevance for risk assessment and regulation

Dissolution (rate) and dispersion stability are relevant triggers needed for the safety assessment of nanomaterials. The information requirements for solubility, dissolution rate and dispersion stability of nanomaterials exist already in some chemical legislations such as REACH (EU 2018). As mentioned above these measurement variables are also relevant triggers for further assessment strategies, but may also contribute to regulatory decisions. Based on the current worldwide development in chemicals regulations towards improved applicability for nanomaterials (e.g. US EPA, 2016), it is noted that other chemicals legislations will meet the same challenges all over the world. Given the numerous manufactured nanomaterials already on the market and many more expected in future, the individual testing of hazard and assessment of the risk would be in practise impossible. To overcome this challenge, grouping and read-across approaches of nanomaterials has been identified as one possible tool by OECD (OECD 2016). Grouping and read-across approaches are already established for chemical substances to meet regulatory data requirements (OECD 2007, 2014b). The aim of these approaches is to predict the physico-chemical, toxicological, and fate-related properties of chemical substances based on structural similarities. If adequate evidence of the structural similarity between two chemical forms is found, then it can be possible to transfer available e.g. (eco)toxicological or fate data from one chemical substance to another one.

However, grouping and read-across based on molecular structural similarity alone is not sufficient for any chemical. This is especially important for nanomaterials, as nanoforms of the same chemical composition can have totally different physico-chemical features, e.g. size and shape, and can then show differences in effects and behaviour. To allow an adequate assessment of nanomaterials using grouping and read-across further parameters are necessary to justify such an approach. Hence, beside chemical composition, parameters like morphology, surface properties, and shape as well as reactivity including coatings and functionalizing, but also fate descriptors like dissolution rate or dispersion stability in relevant media are discussed for consideration (e.g. ECHA Guidance Appendix R-6-1 (ECHA 2019)). Thus, the GD is also of special relevance for grouping approaches.

As dissolution (rate) and dispersion stability are relevant parameters triggering fate and behaviour of nanomaterials in the environment, these measurement variables will also provide input data for environmental fate modelling. Models are available e.g. by Meesters el al. 2019. Especially the dissolution rate of nanomaterials is essential in environmental exposure modelling. It enables the distinction between the dissolved and the particulate form of the nanomaterial. This distinction is included in current environmental fate models for nanomaterials, where dissolution is a process by which nanomaterials are transformed from the particulate form to the dissolved form (Meesters et al. 2019). This is an input parameter in environmental fate models to calculate the predicted exposure concentration. Assuming first order kinetics, the dissolution rate constant can be calculated from experimental data.

4 General conclusions

Both dispersion stability and dissolution (rate) are considered to as important measurement variables for defining environmental behaviour and fate of nanomaterials. Thus, for fate assessment as well as for exposure assessment and environmental modelling both endpoints need to be taken into account. These measurements are also important for planning of ecotoxicity tests and for interpretation of environmental relevance of their results.

While TG 318 for dispersion stability is already published (OECD, 2017), currently no validated OECD TG on solubility and dissolution (rate) of nanomaterials is available. Therefore, the GD considers interim advice on determination of solubility and dissolution (rate) using batch tests as well as flow through tests based on available scientific experience. Furthermore, it refers to existing guidance documents related to this endpoint such as the GD 29 (OECD 2001) or the (at this time available) draft of WNT project 3.10. It advices how these documents may support testing while also mentioning their potential limitations for testing nanomaterial solubility and dissolution under consideration of environmental conditions. A possible testing strategy is presented which indicates decision making based on the purpose of testing in the context of environmental fate and ecotoxicity In addition, as ongoing WNT projects on nanomaterials are also dealing with areas of dissolution an interconnection with these projects is made in order to give orientation how to handle this endpoint in the context of these projects.

As support to TG 318 on the dispersion stability of nanomaterials in simulated environmental media, the GD offers important additions. These include *inter alia* expert advice on the determination of heteroagglomeration with other natural occurring particles which features a scenario of higher environmental realism than depicted in TG 318. Based on the strong heterogeneity of existing natural occurring matter which may interact with nanomaterials released to environmental compartments, a validated standard protocol to determine heteroagglomeration is very hard to achieve. As such, the procedure proposed in the GD is currently unique and of central importance.

With the new “GD for the testing of dissolution and dispersion stability of nanomaterials, and the use of the data for further environmental testing and assessment strategies” another important building block for the testing and interpretation of data on dispersion stability and dissolution rate of nanomaterials became available. It supports interpretation and presentation of data coming from TG 318 and furthermore gives interim guidance on determination and interpretation of solubility and dissolution (rate) of nanomaterials in environmental media while the intended TG is still pending. To support interpretation of data on these endpoints for further testing needs for nanomaterials which are strongly influenced from each other, a test strategy is proposed which supports an appropriate testing regime for the nanomaterial under consideration.

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A Appendix

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