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EUROPEAN CHEMICALS AGENCY

GUIDANCE

Guidance on information requirements and chemical safety assessment

Appendix R7-2 Recommendations for nanomaterials applicable to Chapter R7c Endpoint specific guidance

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LEGAL NOTE

Guidance on information requirements and chemical safety assessment
Extracts from Appendix R7-2 Recommendations for nanomaterials applicable to Chapter R7c - Endpoint specific guidance

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NOTE

Please note that the present document is a proposed amendment to specific extracts **only** of *Appendix R7-2 to Chapter R.7c* of the IR&CSA Guidance.

This document was prepared by the ECHA Secretariat for the purpose of this consultation and includes only the parts open for the current consultation, i.e. :

- Section 2.1.1 Aquatic bioaccumulation

- Section 2.1.2 Effects on terrestrial organisms

http://echa.europa.eu/documents/10162/13632/appendix_r7c_nanomaterials_en.pdf (version 1.0 published in April 2012).

The numbering and headings of the sub-sections that are displayed in the document for consultation correspond to those used in the currently published guidance document; this will enable the comparison of the draft revised sub-sections with the current text if necessary.

After conclusion of the consultation and before final publication the updated sub-sections will be implemented in the full documents.

DOCUMENT HISTORY

Version	Changes	Date
Version 1	First edition	April 2012
Version 2	• Update of section 2.1.1. on aquatic bioaccumulation, to explain the general limitations of the Kow as the basis for a waiver for nanomaterials and provide advice on the applicability of the available OECD guidelines; • Update of section 2.1.2 on Effects on terrestrial organisms to provide advice on spiking methods and use of different metrics.	Xxxx 2017

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2 RECOMMENDATIONS FOR ECOTOXICOLOGICAL ENDPOINTS for NANOMATERIALS:

2.1 Specific advice for endpoints

2.1.1 Aquatic bioaccumulation

In the Parent ECHA Guidance, section R.7.10.2 describes the REACH Annex IX information requirements for aquatic bioaccumulation and the use of alternative information when measured data are not available. However, the prediction techniques described in the parent guidance and the use of surrogate information (e.g. the octanol-water partitioning coefficient Kow) applicable for many classes of organic substances, cannot be used to predict bioaccumulation potential of nanoparticles.

Section R.7.10.3.2 of the parent guidance concerns non-testing data e.g. Quantitative structure-activity realationships (QSARs), BCF models based on log Kow and grouping approaches for assessing aquatic bioaccumulation. The use of non-testing approaches such as (Q)SAR approaches in addressing data gaps for nanomaterials is still very limited. In addition to this, the use of such *in silico* models for nanomaterials has also yet to be established or accepted. With regard to nanoparticles, it is not possible to make bioaccumulation estimations based on log K_{ow} or solubility, as explained in the Appendix R7-1 to ECHA Guidance R.7.a [1] Sections 2.2.1, 2.2.2 and 2.2.4. Therefore the use of non-testing approaches for nanomaterials in deriving an assessment of hazard for the environment must be thoroughly scientifically justified. Appendix R.6-1: Recommendations for nanomaterials applicable to the Guidance on QSARs and Grouping provides an approach on how to justify the use of hazard data between nanoforms of the same substance [2].

Section R.7.10.3.4 of the parent Guidance describes other indicators for bioaccumulation potential. This includes a screening approach where potential bioaccumulation can be estimated from the value of the n-octanol/water partition coefficient (K_{ow}). Furthermore, REACH Annex IX 9.3.2 column 2 states that, for instance, a value for log Kow ≤ 3 could be used as a waiving argument to omit the testing of bioaccumation in aquatic species. This approach is not appropriate for nanoparticles, as prediction techniques based on equibrium partitioning do not apply to nanomaterials - as explained in Appendix R7-1 to ECHA Guidance R.7.a Sections 2.2.1, 2.2.2 and 2.2.4. As outlined in OECD 40, the K_{ow} value is not suitable for predicting bioaccumulation and not an appropriate endpoint for the physicochemical characterization of nanomaterials.

Taking into account the above, waiving the information requirement for bioaccumulation in aquatic species based on log Kow, log Koc or other screening methods should always be accompanied with robust technical and scientific justification for the applicability of the test method used.

In vivo tests for aquatic bioaccumulation

The parent guidance section R.7.10.3.1. describes OECD TG 305 Bioaccumulation in Fish [3] : Aqueous and Dietary Exposure as an appropriate *in vivo* test method to fulfill the information requirement set for bioaccumulation in aquatic species in Annex IX 9.3.2.

OECD TG 305 is partially applicable for nanomaterials. It is applicable when the dietary exposure route is followed; the aqueous exposure route resulting in a *bioconcentration factor* (BCF) is not applicable for most of the nanoparticles. BCF is the ratio of the concentration of a substance in an organism to the concentration in water, once a steady state has been achieved. For nanoparticles, a BCF cannot be calculated as no equilibrium will be reached between the organism and the water phase [4] a stable aqueous concentration cannot be

maintained, and therefore no plateau is reached and only uptake can be assessed (OECD N 40, [5], [6] and [7]).

A new OECD Guidance for assessing the apparent accumulation potential for nanomaterials is under development. This guidance, when available, will provide information on how to test nanomaterials via the dietary exposure and on how to measure and quantify the accumulation potential in fish.

In the meantime, if testing of bioaccumulation in aquatic media is not technically feasible, bioaccumulation in sediment and soil may be considered as a part of WoE in the bioaccumulation assessment of nanomaterials. OECD TG 315 Bioaccumulation in Sediment dwelling Benthic Oligochaetes [8] and OECD TG 317 Bioaccumulation in Terrestrial Oligochaetes [9] are in principle applicable for nanomaterials, but expert judgement will be required for performing the bioaccumulation tests and interpreting the results ([7], [10]). The results of applying these TGs (OECD TG 315 and OECD TG 317), taking into account the current challenge in testing bioaccumulation of nanomaterials in fish, may be used as WoE in bioaccumulation assessment. Soil and sediment compartments are considered potential sinks for nanomaterials and therefore to also be relevant when considering nanomaterial fate in the environment.

Whenever tests for bioaccumulation in fish or sediment and soil organisms are performed, in order to be considered reliable, the recommendations on sample preparation and ecotoxicity and fate testing given in Appendix R7-1 to chapter R7a, section 2.1.1. (Sample preparation) and Appendix R7-1 to R7b, section 2.1 (General advice on how to perform nanomaterials ecotoxicity and fate testing) should be followed. In addition, test concentrations should be monitored throughout the whole test duration to account for concentration-specific changes in dispersion and agglomeration/aggregation characteristics ([11], [7]).

2.1.2 Effects on terrestrial organisms

2.1.2.1 Non testing data

In the parent guidance R7c, part a) of Section R.7.11.3.1, the possibility of using non-testing approaches e.g. QSAR, grouping and the equilibrium partitioning method (EPM) to estimate terrestrial toxicity is explained. Regarding nanomaterials, estimates based on “partitioning” are limited to distribution of a substance in molecular form. In the case of nanomaterials, the partitioning method may underestimate exposure in soil and sediment environments and overestimate the exposure in water. If the particle size is small, distribution via air may also occur. There are no estimation methods available for particle distribution, so this has to be dealt with on a case-by-case basis.

The use of non-testing approaches such as (Q)SAR approaches in addressing data gaps for nanomaterials is very limited at this time. In addition, the use of *in silico* models for nanomaterials has yet to be established or accepted. Therefore the use of non-testing approaches for nanomaterials in deriving an assessment of hazard for the terrestrial environment must be thoroughly and scientifically justified. Appendix R.6-1: Recommendations for nanomaterials applicable to the Guidance on QSARs and Grouping provides an approach on how to justify the use of hazard data between nanoforms of the same substance.

2.1.2.2 Testing data

General recommendations for Ecotoxicological and fate testing (including this endpoint) are given in Section 2.1 of the Appendix on nanomaterials for Chapter R7b.

Regarding testing on effects on terrestrial organisms, the methods described in the parent guidance Section R.7.11 are in principle applicable for testing nanomaterials.
The application technique in e.g. sample preparation and spiking has been shown to have an effect on the availability of the nanomaterial and its level of ecotoxicity in soil ([5]). Therefore it is essential that the sample preparation and spiking method applied is well justified and reported in detail, and that the recommendations set in the OECD Guidance Manual for the

Testing Manufactured Nanomaterials: OECD's Sponsorship Programme; first revision [12] (OECD, 2009), Guidance Notes on Sample Preparation and Dosimetry for nanomaterials [13] and OECD 40 [14] are followed.

When performing the test, the test material needs to be homogenously dispersed in the soil. OECD 40 [14] describes different spiking methods; particles can be dispersed as aquatic dispersion into soil (wet spiking) or directly into test media (dry spiking), or put onto a carrier e.g. silica sand or spiked food. The optimal spiking method depends on both the test material and the test method. It will depend on the physicochemical properties of the nanomaterial, the target concentration, the medium, and the bioassay method selected, and preliminary data gathered prior to the test.

Nano-specific metrics such as particle number and surface area should in principle be used when performing the test as well as the mass metric, unless the use of only mass metric can be justified (see Section 2.1.1 of Appendix to Chapter R7.b).

In addition to these recommendations, it should be considered that measurements of the nanomaterial's concentration (using different metrics) should be monitored throughout the test at all test concentrations to account for concentration-specific changes in dispersion and agglomeration/aggregation characteristics if possible ([11], [7]).

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