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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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Appendix R7-2: Recommendations for nanomaterials

1. INTRODUCTION TO APPROACHES TAKEN FOR APPENDICES CONCERNING INFORMATION REQUIREMENTS

The three appendices concerning information requirements (appendices to R7a, R7b and R7c) have been developed in order to provide advice to registrants for use when preparing registration dossiers for nanomaterials[1]. The content of the appendices implements the advice provided by the REACH Implementation Project on Nanomaterials 2 (RIP-oN2) on specific aspects of information requirements concerning materials in nano form.

The final report of the RIP-oN2 project contains a large amount of information including within its scope applicability of the methods, research gaps etc. This appendix implements only the agreed outputs (i.e. the recommendations for guidance update on which there was consensus).

In the appendices only guidance on the endpoints for which a recommendation has been made in the RIP-oN2 report is included. In the absence of any specific recommendation, either because the endpoint is not relevant for nanomaterials (e.g. flash point or surface tension), or the guidance already provided is considered to be equally applicable to nanomaterials or because more research is needed before developing advice, no additional guidance for the endpoint has been included in this appendix.

Note that new parameters or endpoints (such as ventilation rate, or gill pathologies) have been proposed only when these were explicitly recommended to be included as guidance updates in RIP-oN2.

For further information (e.g. recommended further research & development or reasoning for the advice provided for guidance updates, the reader can refer to the final report of RIP-oN2. (http://ec.europa.eu/environment/chemicals/nanotech/index.htm).

[1] See Recommendation on the definition of nanomaterial adopted by the European Commission

2. RECOMMENDATIONS FOR ECOTOXICOLOGICAL ENDPOINTS ARISING FROM RIP-oN 2 for NANOMATERIALS:

2.1 Specific advice for endpoints

2.1.1 Aquatic bioaccumulation

Section R.7.10.3.2 concerns non-testing data for assessing aquatic bioaccumulation. With regard to nanomaterials, it is not possible to make log K_{ow} or solubility estimations since nanomaterials are dispersed and not in solution. Measured BCF values are required and it is of vital importance to consider changes in e.g. aggregation and agglomerate size. There is furthermore a need to emphasise that for nanomaterials that undergo dissolution such as metallic Silver Ag^0 it is very important to obtain information, if possible, on the form of the substance present in the animal tissue. The use of non-testing data such as read-across, grouping or (Q)SAR approaches in addressing data gaps for nanomaterials is very limited at this time. In addition to this the use of such *in silico* models for nanomaterials has also yet to be established or accepted. Therefore the use of non-testing approaches for nanomaterials in deriving an assessment of hazard for the environment must be scientifically justified.

2.1.2 Effects on terrestrial organisms

2.1.2.1. Non testing data

In general, there are few data available on terrestrial toxicity. In part a) of Section R.7.11.3.1, the possibility of using non testing-data to estimate this endpoint is explained. Regarding nanomaterials, estimates based on “partitioning” are limited to distribution of a substance in molecular form. However, substances may also be distributed in the environment as particles (caused by abrasion/weathering of anthropogenic materials) and hence extrapolation based on partitioning may not be relevant. In such a case the partitioning method may underestimate exposure of soil and sediment environments and overestimate the exposure of water. If the particle size is small air distribution 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 data such as read across, grouping or (Q)SAR approaches in addressing data gaps for nanomaterials is very limited at this time. In addition to this the use of such *in silico* models for nanomaterials has also 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 scientifically justified.

2.1.2.2. Testing data

Regarding testing data (part b of Section R.7.11.3.1), with regard to nanomaterials, the recommendations set out in the OECD Guidance Manual for testing (OECD, 2009) and Preliminary Guidance Notes on Sample Preparation and Dosimetry for nanomaterials (OECD, 2010) need to be taken into consideration, especially in regard to methods of suspension, method of nanomaterials introduction, storage and stability of test material, chemical composition of the test media, characterisation of stock dispersions, characterization of samples (prepared from stock dispersions) prior to administration/testing and if possible during and/or at the end of the test. Explanations should be provided as to why on site monitoring could not be achieved

2.1.3 Guidance on Toxicokinetics

The standard information requirements requested by REACH (Annex VII) can give useful information to make judgements about the possible toxicokinetics of substances (See Section R.7.12.2.1). It is possible that the physico-chemical characteristics of the substance will change if the substance undergoes metabolic transformation or other physical or chemical

modification **in the test** system and the physico-chemical characteristics of the parent substance may not provide any clues as to the identity, distribution, retention and elimination of its metabolites. In the case of nanomaterials special attention should be given to possible changes in the test system.

Regarding gastrointestinal absorption (Appendix R.7.12-2- Prediction and toxicokinetics integrating information generated *in silico* and *in vitro*), in order to be absorbed from the GI tract, substances have to be present in solution in the GI fluids, and from there have to cross the GI wall to reach the lymph or the venous portal blood. In the case of particulates, the possibility for small sized particles in the nanometer size range to translocate[2] across the GI wall in particulate form should be considered.

[2] Please note that translocation can occur also for other uptake routes.

REFERENCES

OECD. 2009, "Guidance manual for the testing of manufactured nanomaterials: OECD's sponsorship programme. First revision", Series on the safety of manufactured nanomaterials, ENV/JM/MONO(2009)20/REV, Paris.

OECD. 2010, "Preliminary Guidance Notes on Sample Preparation and Dosimetry for the Safety Testing of Manufactured Nanomaterials", Series on the safety of manufactured nanomaterials, ENV/JM/MONO(2010)25, Paris.

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