Bundesanstalt für Arbeitsschutz und Arbeitsmedizin

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Multi-walled Carbon Nanotubes (MWCNT), synthetic graphite in tubular shape and tangled

EC No 936-414-1/701-160-0

Evaluating Member State(s): Germany

Dated: 10 July 2020

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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2019

Germany concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Multi-Walled Carbon Nanotubes (MWCNT) were originally selected for substance evaluation in order to clarify concerns about:

- Wide spread use
- Consumer use
- Discrepancy in self-classification between different registrants of the joint submission(s)
- Differences in physico-chemical properties that affect toxicity, i.e. number of different registered nanoforms and the choice of representative test material(s)
- Suspected STOT RE (differing NOAEL/Cs in several animal studies using different forms of the same test material)
- Suspected carcinogen
- Effects on environmental organisms
- Suspected environmental exposure
- Cumulative exposure
- Suspected persistency

During the evaluation the eMSCA identified further concerns for most of the examined Human Health (HH) endpoints (cf Table 3) precluding final conclusions with regard to the hazard assessment of the substance. The concerns included insufficient read-across justifications, lack of (standard) information, methodological deficits, as well as insufficient clarification of potential hazards. However, the eMSCA acknowledges the partially considerable differences in terms of completeness between individual registrations and data submitted for specific MWCNT types and nanoforms. Nevertheless, registered MWCNT have been appraised collectively as substance under evaluation in this document.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There are no other on-going or concluded processes at EU-level for the registered substance.

A CLH proposal for rigid MWCNT with WHO fibre dimensions[2] according to Carc. 1B (inhalation route) and STOT-RE 1 (lung) has been submitted to ECHA by the DE CA in 2019.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

In the framework of the substance evaluation it was not possible to resolve the concerns described under 1. Furthermore, to some extent the substance evaluation revealed additional indications supporting the initial concern. Moreover it appears that in the dossiers it is not made transparent which data is appropriate for which nanoform(s).

[2] Length > 5 µm, diameter < 3 µm and aspect ratio (length/diameter) > 3

Based on these ambiguities regarding the registered nanoforms as well as based on the late updates of some of the dossiers at the very final stage of the substance evaluation, it does not seem expedient to conclude on the substance evaluation with a decision on data requests at the present time.

Based on the amendment of the REACH regulation by Regulation (EU) 2018/1881 of 3 December 2018 additional information is required for nanomaterials since 01.01.2020. In the opinion of the eMSCA, these information requirements were not (adequately) addressed by the registrants yet. Thus, further action is needed.

According to 46 (4) of REACH, substance evaluation is concluded after 12 months with no possibility for extension in case no draft decision with further information requirements is submitted to ECHA. However, a *de novo* substance evaluation is still possible at a later stage.

Currently, the eMSCA considers it necessary for ECHA to first examine if all information according to REACH Annex VI are available within the framework of a compliance check. In case of missing information, these data should be requested by respective decisions.

Once this information is available, it has to be decided if further information is needed to clarify a remaining concern and if this should be requested in the framework of a compliance check or a substance evaluation.

Apart from potential requests as consequences of a compliance check, the registrants are urged to update their dossiers and/or develop testing proposals in order to adhere to the requirements of the REACH Regulation (including the amendments by Regulation (EU) 2018/1881).

Table 1

CONCLUSION OF SUBSTANCE EVALUATION Conclusions	Tick box
Need for follow-up regulatory action at EU level	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
Currently no need for regulatory risk management follow-up action at EU level; Outcome of compliance check needs to be awaited first.	x

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not possible for the time being. Compliance check is needed first (see section 3).

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Compliance check	tbd	ECHA
Potential inclusion to CoRAP for resuming Substance Evaluation	tbd	DE-CA

The need for a re-opening of the Substance Evaluation process will be determined based on the outcome of the new information generated via the Compliance Check procedure.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

MWCNT were originally selected for substance evaluation in order to clarify concerns about:

- Wide dispersive use;
- Consumer use;
- Discrepancy in self-classification between different registrants of the joint submission(s);
- Differences in physico-chemical properties that affect toxicity, i.e. number of different registered nanoforms and the choice of representative test material(s);
- Suspected STOT RE (differing NOAEL/C/s in several animal studies using different forms of the same test material);
- Suspected carcinogen;
- Effects on environmental organisms;
- Suspected environmental exposure;
- Suspected persistency;
- Cumulative exposure.

During the evaluation the eMSCA identified further concerns for most of the examined endpoints (cf Table 3) precluding final conclusions with regard to the hazard assessment of the substance. The concerns included insufficient read-across justification(s), lack of (standard) information, methodological deficiencies as well as insufficient clarification of potential hazards.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Acute aquatic toxicity	Some studies available, unclear whether the available information can be considered relevant and representative for the registered MWCNT nanoforms.
Chronic aquatic toxicity	Limited information available, unclear whether the available information can be considered relevant and representative for the registered MWCNT nanoforms.
Sediment/Soil toxicity	No information available as the endpoint is waived by the registrants. However, according to the eMSCAs assessment exposure cannot be excluded.
Toxicokinetics	The available data for inhaled or orally administered MWCNT is insufficient (including standard data gaps) and

	inconclusive. Moreover, it is unclear whether the available information can be considered relevant and representative for all registered MWCNT nanoforms.
Acute toxicity	Choice of test substance insufficiently justified, thus questioning the representativeness for all registered MWCNT nanoforms. Partially, dosimetry of inhalation testing was incompliant with OECD TGs.
Skin sensitisation Respiratory sensitisation	Few nanoforms negatively tested for skin sensitisation but read-across justification insufficient, precluding representativeness to all registered nanoforms. Methodological deficiencies observed and poor characterisation information of (some of) the different tested/registered MWCNT forms. There are no robust data on the respiratory sensitising potential of MWCNT. However, literature data suppose an aggravating potential in individuals with signs of respiratory sensitisation.
Repeated dose toxicity (inhalation)	Hazard concerns related to inflammogenic local and systemic toxicity have been identified, partially already at low exposure concentrations. The hypotheses of generic volume-based particle overload of the lung as principle driver of toxicity ignores the variability of the registered nanoforms in terms of morphology, biopersistence and metal contaminants. Representativeness of the test substance for all registered nanoforms lacks justification. Large NOAEC/LOAEC ranges across registrations suggest differences in nanoforms and/or methodological incompliance. Corresponding derived DNELs need re-consideration.
Repeated dose toxicity (oral)	Submitted data is insufficient and with methodological deficiencies, impairing the conclusion whether some/all registered MWCNT can elicit systemic toxicity. Data from the scientific literature is inconclusive. It is also unclear whether the available information is relevant and representative for all registered MWCNT nanoforms.
Repeated dose toxicity (dermal)	No data submitted for any of the registered MWCNT forms.
Mutagenicity	The submitted data is inconclusive and insufficient for a proper hazard and risk assessment. It is unclear whether the available information is relevant and representative for all registered MWCNT nanoforms. For some of the registered nanoforms a potential hazard cannot be excluded based on comparative data in the scientific literature.

Carcinogenicity	No data for any of the registered MWCNT forms available. Subchronic inhalation studies reported progressive fibrosis and lung epithelial tissue proliferation when MWCNT persist in the lung, raising a carcinogenic concern. Fibre-like pathogenicity cannot be excluded for several of the registered nanoforms.
Toxicity to reproduction: fertility	No data was provided for this endpoint. The available reproductive toxicity information in the scientific literature raises a potential concern for reproductive toxicity (fertility). Whether this concern is relevant for all/some/any of the registered nanoforms cannot be evaluated at present due to missing standard data and poor kinetic information.
Toxicity to reproduction: developmental toxicity	Several standard data gaps were identified preventing a proper hazard and risk assessment. Scientific literature information raises a HH concern for developmental toxicity for the registered MWCNT, which however, cannot be verified at present due to missing standard data and insufficient characterisation as well as poor toxicokinetic information of the tested nanoforms.
Exposure of professionals/workers	The available information on worker exposure indicates the potential exposure to be very low for some of the nanoforms, but is in general terms insufficient to conclude on the resulting exposure at the workplace for all nanoforms.
Exposure of consumers	The available information on the application of the substance and resulting consumer exposure is currently insufficient for the eMSCA to exclude consumer exposure. A potential low consumer exposure would be taken into account to ensure precaution in a subsequent risk assessment.
Environmental exposure	The available information on use, fate and behavior is insufficient to conclude on environmental exposure.

7.2. Procedure

MWCNT have been included in the Community Rolling Action Plan (CoRAP) in 2015. The evaluation started officially with the publication of the CoRAP 2019 – 2021 on 19 March 2019.

Before the formal start of the evaluation the eMSCA contacted all registrants in order to bilaterally gather additional information on the individual forms of MWCNT registered (such as information on characterisation, uses, exposure). The registrants were advised to provide the additional information in an update of their registration dossiers. Most of the registrants followed this advice. Further bilateral contact with some registrants was sought during the year of evaluation where necessary.

On 01 January 2020 the new information requirements on nanoforms of substances as introduced into the REACH Regulation by Regulation 1883/2018 entered into force,

requiring the registrants to submit updates of their registration dossiers with additional information on their nanoforms. Hence, updates of some of the registrations were received very late in the process and could not be assessed thoroughly before the end of the year of evaluation.

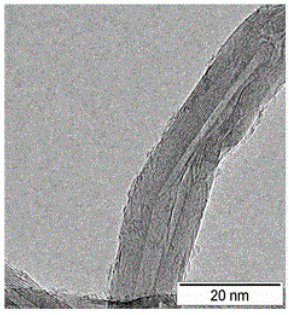
The substance evaluation was concluded on 19 March 2020 without clarification of the concern due to the reasons stated above. At the same time the eMSCA suggested that Compliance Checks should be performed by ECHA.

7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Multi-Wall Carbon Nanotubes (MWCNT), synthetic graphite in tubular shape
EC number:	936-414-1 / 701-160-0
CAS number:	
Index number in Annex VI of the CLP Regulation:	
Molecular formula:	C
Molecular weight range:	
Synonyms:	Inter alia: Baytubes, Nanocyl TM, Jeno Tube, K-Nanos, Graphistrength

The following depicts an exemplary sample of a MWCNT:



MWCNT fulfil the definition of a nanoform of a substance as included in Annex VI of the REACH Regulation as of 01 January 2020.

Electron microscopy images show that the registered MWCNT consist of tightly bound agglomerates consisting of tangled tubes. Shape of agglomerates differs from more particle-like structures to bundled ("fibrous") structures.

The tubes within the MWCNT agglomerates are described as short, thin and tangled. Specifically, they display an outer tube diameter distribution of at least 90 % below 30 nm (D90 <= 30 nm).

The registrants provided information regarding the length of their MWCNT. It is, however, not clear in some cases whether the individual tube length or the length of the bundles/particles was determined.

Overall, all registrants provided some pieces of information on the characterisation of their MWCNT. However, comprehensive characterisation of the individual nanoforms covered by the different registrations is lacking.

7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	black agglomerated grains, odourless
Vapour pressure	waiving, melting point of the substance is >300°C
Water solubility	<2 mg/L at 20°C, pH 7.5 - 9.2, The result < 2 mg/L refers to the limit of quantification (LOQ) of the detection method for total dissolved carbon.
Partition coefficient n-octanol/water (Log Kow)	waiving, substance is inorganic
Flammability	non flammable
Explosive properties	non explosive
Oxidising properties	No (according to Lead registrant)
Tube dimensions	boundary: diameter d90*: ≤30 nm, length < 5 µm**
Stability in organic solvents and identity of relevant degradation products	waiving, substance is inorganic
Dissociation constant	waiving, the substance does not contain any functional groups that may dissociate

* an outer tube diameter distribution of at least 90 % is under 30 nm (D90 <= 30 nm)
** This is the length of a single MWCNT. However, the length of single tubes of several registered MWCNT forms was not determined.

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☒ 100 – 1000 t	☐ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Table 7

USES Use(s)	
Uses as intermediate	-
Formulation	Additive for materials
Uses at industrial sites	Formulation of polymers, manufacture, processing articles
Uses by professional workers	Use leading to inclusion onto/into article, formulation, processing preparations, non reactive processing aid and transfer, which in part are still in the stage of research and development.
Consumer Uses	ECHA has no public registered data indicating whether or in which chemical products the substance might be used.
Article service life	Used in complex articles with no intended release. Applied in plastic, rubber, stone, cement, glass, ceramic and metal products

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

There is currently no harmonised classification of tangled MWCNT. The DE-CA submitted a CLH proposal for rigid MWCNT with WHO fibre dimensions[3] proposing a classification as Carc. 1B (inhalation route) and STOT-RE 1 (lung) to ECHA in 2019.

7.6.2. Self-classification

EC 701-160-0: Eye Irrit (H 319) and STOT SE 3 (H 335).
EC 936-414-1: No self-classification

7.7. Environmental fate properties

Only very few studies are available on environmental fate properties in the registration dossiers. Limited information is available on bioaccumulation and dispersion stability. However, the provided information is incomplete and not reliable and, therefore, it stays unclear how other registered forms of MWCNT are covered by these data. All other environmental fate endpoints were waived by the registrants for different reasons (inter alia, the information is claimed to be "not relevant" or "technically not feasible"). Based on the amendments of the REACH annexes for registration of nanomaterials, relevant endpoints for determining fate and behaviour of nanomaterials in the environment have to be covered and are needed for risk assessment. These include dispersion stability and dissolution in environmental media. Thus, in case of environmental fate properties, the eMSCA recognizes important data gaps in standard information requirements for the MWCNT forms registered.

[3] Length > 5 µm, diameter < 3 µm and aspect ratio (length/diameter) > 3

7.8. Environmental hazard assessment

The registration dossiers include aquatic toxicity data on MWCNT and some acute and very limited chronic information. With the new obligation under REACH applicable from 01.01.2020 chronic toxicity data instead of acute toxicity data are required to report on the aquatic toxicity of nanoforms. Based on the insufficient characterisation information provided by the registrants it is not possible to conclude whether or not all forms are adequately addressed by the available studies. Within the dossiers various forms of MWCNT as well as pooled nanoforms are registered. For some endpoints read across were performed between nanoforms or within pooled nanoforms without (adequate) justification. Furthermore, justification and definition of these pooled nanoforms are missing. It has to be anticipated that based on the range of physical chemical properties (e.g. diameter or number of walls, length, functionalisation or impurities) exhibited by the registered MWCNT forms, variations in behaviour, fate, aging and toxicity in the environment may occur. However, convincing hypothesis why ecotoxicity data of the investigated forms is valid to represent toxicity of all other forms of the registration is missing. Thus, from the perspective of the eMSCA, standard information on aquatic ecotoxicity is missing. Only if these standard information for all registered forms is available (either by providing data for all registered forms or by deriving adequately justified grouping concepts with evidence for representative toxicity data for groups of MWCNT), it is possible to properly assess the potential aquatic toxicity of the registered MWCNT and thus, to conclude whether or not regulatory action is needed.

No data on sediment or soil toxicity are included in the registration dossiers. These endpoints were waived for different reasons, inter alia, that no exposure is expected. However, based on the available information, the eMSCA cannot exclude exposure to soil and sediment. In addition, more uses than given in the registrations are expected which could lead to potential release into the environment (including soil). Therefore, the eMSCA considers that data on soil organisms might be required for those MWCNT manufactured or imported in the respective tonnage band.

7.9. Human Health hazard assessment

The registration dossiers comprise a considerable number of different forms of MWCNT. Endpoint-specific information has been covered by studies generated on a limited number of MWCNT forms, and supplemented by published data which tested registered or other nanoforms. However, because of incomplete characterisation of information across the various registered MWCNT, and lack of or insufficient read-across justification(s), it is not possible to conclude whether or not all registered forms are adequately represented by the available testing data. Moreover, comparative toxicokinetics and toxicity data is scarce or if available show marked differences between nanoforms, which might be due to important known drivers of toxicity, such as dimension, shape, functionalisation and type and amount of impurities. Based on this information, differences in kinetic behaviour and toxicity between distinct forms of MWCNT can be expected. Therefore, the eMSCA does not concur with the presumed equivalence of all tangled MWCNT, as well as the assumption of particle dust overload being the sole relevant trigger of inhalation toxicity. Accordingly, the eMSCA also questions that the few tested MWCNT forms are representative for all of the registered MWCNT forms, irrespective of their different physico-chemical properties.

Overall, based on the available data the eMSCA identified several hazard-based concerns, which however cannot be addressed within this SEv process, because of i) lack of clarity regarding the consideration of MWCNT forms according to set boundary criteria, ii) missing or insufficient grouping/read-across justification(s) in terms of test material selection and representativeness thereof, and iii) standard information gaps and/or inappropriateness of test design(s). It is the eMSCAs opinion that adequate assessment presupposes complete fulfilment of characterisation information requirements according

to the recently revised REACH Annex VI, which is active since 01 Jan 2020, in order to be able to assess the similarity of nanoforms and their equivalence, including the verification of sets of nanoforms. Thus, these issues should be addressed in a dossier evaluation first and the new and complete data set should be evaluated subsequently with respect to potential human health risks to eventually conclude whether a second SEv should be initiated.

7.9.1. Toxicokinetics

With adaptation of the REACH Annexes in 2020, in the 10-100 tonnage band a toxicokinetic study shall be proposed or may be required by the Agency in accordance with Article 40 or 41 in case such an assessment cannot be performed on the basis of the relevant available information (REACH Annex 8.8.1). The eMSCA notes that available information for assessment is limited and lacks read-across justification(s) for the various registered forms of MWCNT that were not tested.

Regarding inhalation, the available data is insufficient and inconclusive with regard to clearance, accumulation of MWCNT in and translocation from the lung and lung-associated lymph nodes (LALN). Comparability is further limited due to differences in sample preparation.

In terms of oral exposure, systemic effects were observed in respective repeated dose toxicity studies, suggesting translocation of MWCNT from the gastrointestinal tract (GIT), whereas tracing/tracking studies with different MWCNT did not find evidence for translocation via the GIT. However, when administered intravenously, these MWCNT types accumulated differently in liver, spleen and lung (Jacobsen et al., 2017). Reliable route-specific toxicokinetic information on translocation by the MWCNT forms covered by the registration(s) is important, in order to be able to safely exclude any accumulation of the substance and chronic systemic effects in non-pulmonary target organs and, thus, enable a proper risk assessment.

7.9.2. Acute toxicity

The eMSCA notes that as of January 1, 2020, the updated REACH-Annexes have become effective, i.e. for nanoforms, inhalation is the default route for standard acute toxicity testing. Accordingly, waiving would need particular justification.

A few OECD test guideline (TG) 403 inhalation studies have been submitted, testing a limited number of the registered nanoforms. Justification(s) for the representativeness of the test substances for the respective registration was either not provided or is considered insufficient. Test concentrations varied considerably, indicating underdosing in some of the studies.

Submitted oral studies, which tested some of the registered nanoforms, revealed – among other inflammatory effects – the occurrence of inflammatory granuloma in liver, indicating possible translocation of the tested MWCNT from the GIT into systemic circulation. The majority of the oral studies used dosages below those required according to corresponding OECD TGs. This deviation from the TG specifications was justified with poor dispensability of MWCNT in aqueous medium.

Regarding the dermal route, no acute toxicity was observed up to 2000 mg/kg for those nanoforms tested, despite deviations of OECD TG 402 in terms of sample preparation, as the test material was used without moistening using a suitable vehicle and dermal discoloration by the MWCNT that might have masked cutaneous reactions.

Altogether the provided information is considered insufficient to conclude on acute toxicity for all registered MWCNT.

7.9.3. Sensitisation

Skin sensitisation

Human data on the skin sensitising potential of MWCNT is not available. Some registrants submitted negative animal testing data on the sensitising potential of MWCNT, comprising a Local Lymph Node Assay (LLNA), a guinea pig maximisation test (GPMT), and a Buehler test. Two MWCNT nanoforms were tested in total, one of which was a non-marketed, poorly characterised MWCNT, used without further justification of representativeness of the test material. Likewise, read-across justification(s) to other non-tested registered nanoforms were either missing completely or, if available, deemed inacceptable (because of high amounts of single-walled carbon nanotubes (SWCNT) in the test substance). Furthermore, tests deviated from OECD TGs (e.g. administration issues, epicutaneous induction instead of intradermal induction, powder vs. dispersion testing) or were conducted with relatively low concentrations of the test substance, impairing the robustness of the test results.

All in all, although none of the submitted data revealed a skin sensitising potential of the tested MWCNT due to the poor characterisation of the non-tested registered MWCNT and the missing and/or insufficient read across justification(s), the eMSCA concludes that there are standard information data gaps for this human health endpoint, which should be addressed in dossier evaluation. The necessity of a case-by-case approach is underpinned by the fact that registered MWCNT forms markedly differ in amount of metal impurities, among which are known sensitisers (see also 7.9.11).

Respiratory sensitisation

One registration included data on respiratory sensitisation for one form of registered MWCNT. The tested MWCNT form was not a respiratory sensitiser by itself but dose-dependently aggravated a systemic immune response and airway inflammation, mucus production, and fibrotic response in previously sensitised mice (Ronzani et al., 2014). Literature data on several MWCNT nanoforms support this finding, by indicating that individuals who exhibit signs of respiratory sensitisation, e.g. asthma, may be more susceptible to adverse effects from chronic MWCNT exposure than healthy individuals (Chortarea et al., 2017; Hansen et al., 2014a; Ihrie et al., 2019; Inoue et al., 2009; Mizutani et al., 2012; Nygaard et al., 2013). However, other studies show contradictory results (Staal et al., 2014). Currently, no formally recognised and validated tests exist for respiratory sensitisation. Furthermore, human data addressing the respiratory sensitisation of MWCNT is lacking. The available data is not sufficient for classification of MWCNT as respiratory sensitiser. However, as stated above, the (skin) sensitisation potential of individual MWCNT nanoforms due to metal contaminants is unknown, which raises a health concern.

7.9.4. Repeated dose toxicity

Inhalation

Some information from subchronic OECD TG 413 and subacute OECD TG 412 studies in rats which tested some of the registered nanoforms (including a no longer commercialised material) is available. In case adverse effects were reported they were either considered incidental or generic due to particle-like overload exclusively and thus reversible. None of the studies reported systemic effects beyond the lungs. NOAECs/LOAECs from these studies were crucial as points of departure (POD) for DNEL derivation and hazard assessment by the registrants.

The eMSCA does not agree with the registrants' conclusions based on the available data and derived effect values. Local effects, attributed to a foreign material-induced inflammatory response in the lung became manifest already at low concentrations and were only partially reversible. Low concentration effects were explained by volumetric

overload of loosely packed particle like structures, negating any substance-dependent effects. However, it cannot be excluded that substance properties such as morphology, size, surface area and metal contaminants affect cellular interaction(s), and uptake and fate, contribute to compromised lung clearance resulting in persisting inflammation and detrimental effects on target cells. Furthermore, differences in aerosol generation may have a substantial impact on the test outcome, as discussed by the registrants themselves (e.g. shape, share of respirable particles, changes in oxidation potential). Accordingly, the eMSCA does not agree with the generic mode of action hypothesis of the registrants, considering the variability in physico-chemical properties of the registered MWCNT and test aerosol generation.

The paucity of available toxicokinetic information (see section 7.9.1) increases this uncertainty. Lung burden measurements were rarely performed, rather described qualitatively as discoloration of the lungs. Translocation beyond the respiratory tract was negated. However, tracing experiments faced stability and detection limit issues, and qualitative analysis of discoloured tissue lacked sensitivity and completeness with regard to non-pulmonary organs. Frequently, inhaled MWCNT were found in LALN indicating clearance and/or translocation. The scientific literature describes systemic effects by inhaled MWCNT, affecting the cardiovascular, the neuronal and the immune system (see section 7.9.8). It is not clear if the effects are caused by bioavailable MWCNT, leached metal contaminants, or secreted inflammatory mediators. In any case, the eMSCA deems this a health concern, which is not sufficiently addressed by the registrants, not the least because information regarding chronic inflammation and physiological consequences are missing.

The eMSCA further notes that several of the registered MWCNT fulfil WHO fibre criteria[4] especially with regard to the length (< 5 µm) in addition to their very high biodurability raising a fibre pathogenicity/carcinogenicity concern upon chronic inhalation. This is particular true in case when nanotube agglomerates form aligned bundles.

NOAECs partially differed markedly among the tested MWCNT types, which might be due to both, differences in physico-chemical properties of the test materials and differences in aerosolisation (affecting their respirability).

Additional shortcomings identified by the eMSCA included: i) unjustified deviations from test designs of the revised OECD TGs 412 and 413 with regard to dosimetry, exposure duration and lung burden measurements, ii) insufficient characterisation of test aerosols and reporting of deviations to specification of the registered substance(s), and iii) missing or insufficient read-across/grouping justification(s) for the other forms covered by the registration(s).

The eMSCA concludes that the provided information is insufficient to allow concluding on repeated inhalation toxicity for all registered MWCNT.

Oral administration

The registration dossiers include two (subacute) repeated dose studies via the oral route. The eMSCA deems the information received insufficient for the following reasons:

- Non-guideline studies
- Poor documentation of methods and results
- Nanoforms tested w/o providing any read-across/grouping justification

[4] Length > 5 µm, diameter < 3 µm and aspect ratio (length/diameter) > 3

- Contradictory results: No (local, systemic) effects vs. systemic (liver) toxicity, indicating distinct translocation behaviour and resulting in very different NOAELs

- No direct comparison of results possible due to marked differences in study designs (e.g. gavage vs. diet, use of different vehicles, etc.), making it impossible to currently conclude on the potential drivers of oral toxicity.

However, adverse liver effects were also observed after repeated oral administration of a similar MWCNT form to the registered MWCNT in a study by Fang et al. (2018). Moreover, additional adverse effects of tangled MWCNT via the oral route were identified in the scientific literature (Chen et al., 2018; Vasyukova et al., 2015); these effects include reproductive toxicity, effects on the abundance, composition and diversity of gut bacteria, inflammation of the GIT, as well as signs of an increased intestinal permeability. Although included in the registration, no data on oral repeated dose toxicity of surface-modified MWCNT is available, preventing a firm conclusion on potential hazard concerns.

In summary, the available oral toxicity information shows that there is a potential human health concern by tangled MWCNT which however cannot be resolved at present, due to the insufficient characterisation of various registered nanoforms, and as in general data on physico-chemical characteristics, impurities/composition and agglomeration behaviour in different vehicles, etc., is rather limited in the available studies. Moreover, the available data lacks compliance with currentlyvalidated OECD TG requirements and comparative data for the different MWCNT forms is lacking.

Dermal administration

No data on dermal repeated dose toxicity are available.

Other routes

No data are available in the registrations. Relevant information, however, was obtained from the scientific literature. Single or repeated intravenous (IV) injection(s) (Jain et al., 2011; Lacerda et al., 2008; Zhang et al., 2017b) reported liver toxicity similar to those observed after repeated oral administration. Similarly, single or repeated IV injection(s) of surface modified MWCNT (i.e. COOH-MWCNT) resulted in adverse effects on liver and the gut microbiome in several studies (Adedara et al., 2018; Chen et al., 2013a; Jain et al., 2011). Results indicate that MWCNT can pose a human health risk if they become systemically available. Whether the reported effects are relevant (i.e. non-natural exposure route) and representative for the registered forms of MWCNT, however, remains questionable due to the insufficient data available.

7.9.5. Mutagenicity

The registrants concluded absence of genotoxicity of tangled MWCNTs based on the various in vivo and in vitro studies available in the dossier(s). The eMSCA can only partially follow this conclusion, as i) only a few of the registered nanoforms were actually tested, ii) justification(s) that the tested materials serve as reference for the other registered forms, have either not been delivered, or if available, are considered insufficient and iii) methodological deficiencies were identified.

In vitro

Regarding *in vitro* mutagenicity data, a number of negative Ames tests (OECD TG 471) were provided for some of the registered MWCNT. These studies were referenced as key

studies, reliable without restrictions. According to OECD 43 (2014)[5], 'The use of the Ames test (TG 471) is not a recommended test method for the investigation of the genotoxicity of nanomaterials'. Based on this, it is advisable that any negative data harvested from such bacterial mutation tests should be followed up with other assays after the initial screening, perhaps via implementation of a battery of standardised genotoxicity testing methods covering an as wide as possible variety of potential genotoxic mechanisms. In addition to the use of other assays, determination of cellular uptake by appropriate methods will help in the interpretation of in vitro genotoxicity assays.

With regard to the mammalian cell gene mutation potency of MWCNT, available data are inconclusive for some registered nanoforms either because the read-across justification(s) was/were insufficient or because it was completely lacking. Additionally, the impact of metal contaminants was not considered (e.g. by assay modifications to detect oxidative DNA damage or selection of highly purified test materials instead of commercialised MWCNT types). This is of particular importance, as several of the listed impurities of some forms of the registered MWCNT are known genotoxicants.

It is further noted that some of the submitted *in vitro* studies assessing the clastogenic effects of the tested MWCNT exhibited methodological deficiencies (e.g. regarding the choice of controls, nanomaterial specific adaptation such as prolonged incubation time, acceptability criteria not met in terms of historical positive and negative controls). Moreover, various studies used different cell types, and variations in sample preparation and assay performance were reported, precluding comparability of the results (NANOGENOTOX, 2013[6]). Therefore, the eMSCA considers that the provided studies cannot resolve/eliminate the potential genotoxicity concern.

In vivo

The registrants provided in vivo studies testing for DNA and chromosomal damage, respectively, as well as for the mitotic apparatus of erythroblasts without justification for the selection of the test material. The studies state guideline conformity although major flaws were identified in several studies regarding choice of dose levels, route of administration, statistical evaluation, and reachability of target tissues. Therefore, the eMSCA is disregarding these studies for the hazard assessment of MWCNT.

Another concern was identified by the eMSCA when reviewing the scientific literature, namely the potential indirect genotoxicity via the generation of reactive oxygen species (ROS) upon interaction with cellular compartments (e.g. mitochondria or cell membrane) (Cao et al., 2014; Kim et al., 2014; Kim et al., 2012; Knudsen et al., 2019; Poulsen et al., 2013; Poulsen et al., 2015). Based on the provided data it is not possible to exclude oxidative DNA damage of the registered MWCNT. Furthermore, an aneugenic and clastogenic potential of some of the registered nanoforms was reported in the literature data included in the registration dossier(s) (Muller et al., 2008). The registrants rejected the study due to major methodological deficiencies. The eMSCA agrees that there are methodological flaws in this study (e.g. non-physiological route of administration, limitations regarding site-of-contact (lung) genotoxicity). However, as the results were positive, the eMSCA considers this study relevant in a weight of evidence approach.

Overall, the data submitted by the registrants are considered inconclusive. Several positive genotoxicity studies have been ignored by the registrants (Cao et al., 2014; de

[5] http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)34&doclanguage=en

[6] NANOGENOTOX (2013): Facilitating the safety evaluation of manufactured nanomaterials by characterising their potential genotoxic hazard. French Agency for Food, Environmental and Occupational Health & Safety (ANSES). https://www.anses.fr/en/system/files/nanogenotox_final_report.pdf

Jong, 2013; Poulsen et al., 2015). In addition, inhalation and instillation studies with MWCNT forms with similar properties as the registered forms showed positive results (in some cases associated with the generation of ROS). Accordingly, the mutagenicity concern can currently not be resolved for the registered MWCNT forms.

7.9.6. Carcinogenicity

Neither human information nor animal testing data via a physiological route for thin, tangled MWCNT is available. A 2-year inhalation study according to OECD TG 453 reported dose-dependent development of lung carcinomas (but no pleural mesotheliomas) in rats induced by a well dispersed aerosol of MWNT-7 (Mitsui), a high diameter and more rigid material of respirable fibre length (Kasai et al., 2016), under non-overload conditions.

The mode of action of carcinogenicity following MWCNT inhalation is currently discussed (Donaldson et al., 2013; Kasai et al., 2016). According to the fibre pathogenicity paradigm, fibre dimensions and biopersistence are the most relevant critical factors, ultimately leading to lung and pleural cancer, involving incomplete ("frustrated") phagocytosis as key event.

With regard to dimensions, an experimental study employing intraperitoneal (IP) injection failed to induce typical mesothelioma pathogenesis, when tangled MWCNT with a diameter of about 15 nm were administered, despite their high biodurability (Muller et al., 2009). The boundary composition of the MWCNT covered by the registration(s) excludes longer and thicker MWCNT types. Diameter is a critical parameter as it is assumed that MWCNT below 20-30 nm lose their rigid fibre shaped tubes and become increasingly tangled. It is noted that not all registered nanoforms comply with these boundary dimensions, and formation of (aligned) high diameter bundles need to be considered, which would fulfil WHO fibre criteria[7] (see 7.9.4).

Available subchronic inhalation studies on non-rigid (tangled) MWCNT (see section 7.9.4) suggest that a generic volumetric overload of alveolar macrophages leading to their high lung retention is the predominant mode of action in bringing about persistent inflammation resulting in fibrosis and tissue remodelling. In addition, though MWCNT are observed in LALN, direct evidence for translocation is missing.

However, since chronic exposure data for non-rigid MWCNT is not available, substance-related lung tumour induction cannot be excluded. Alveolar clearance can also be compromised by more direct tumour-triggering effects on resident target cells, such as cytotoxicity and genotoxicity, depending on surface reactivity, structural features and contaminants of the MWCNT nanoforms, in particular when cells take those up. On the other hand, fibre pathogenicity is a concern in case assembly structures of MWCNT form rigid aligned bundles. However due to insufficient information of the registered MWCNT in terms of characterisation, toxicokinetics and long-term toxicity, the carcinogenicity concern cannot be clarified at present.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Fertility

One guideline-conform OECD TG 421 reproductive screening study is available in the registration dossiers testing a single form of the registered MWCNT via the inhalation route. As in the RDT inhalation studies with the same test material, severe testes effects were observed in male rats in this study. The significance of these effects, however, is questionable as they are rather common in nose-only inhalation experiments due to the stress associated with immobilization in the restrainer during the inhalation procedure

[7] Length > 5 µm, diameter < 3 µm and aspect ratio (length/diameter) > 3

(Lee et al., 1993). It is noted, that results of the provided oral repeated dose toxicity study with the same test material revealed mild testes effects as well, which cannot be explained by immobilization.

As no guideline-conform reproductive toxicity studies were provided for any of the other registered MWCNT forms, the relevance of these findings for all other registered MWCNT nanoforms cannot be evaluated. The provided waiver(s) for this endpoint are considered invalid. This is of special importance as several studies, which were identified in the scientific literature (Hansen et al., 2014a; Hougaard et al., 2013; Johansson et al., 2017) tested the reproductive toxicity of one of these registered MWCNT forms via intratracheal (IT) administration and reported adverse fertility effects in treated mice.

Further literature data from oral RDT studies testing other (non-registered) tangled MWCNT with similar properties than the registered forms also reported adverse fertility effects (Fang et al., 2018; Vasyukova et al., 2015). Surface-modified tangled MWCNT administered via IT instillation and IV injection, respectively, yielded similar adverse effects in mice and rats (Bai et al., 2010; Farombi et al., 2016; Huang et al., 2014; Mohammadi et al., 2017; Nirmal et al., 2017; Qi et al., 2014) and additional in vitro studies further suggest a reprotoxic potential of relevant MWCNT (Aminzadeh et al., 2017; Qu et al., 2017; Xu et al., 2016).

Taken together, the available reproductive toxicity information shows that there is a potential concern for reproductive toxicity (fertility) of tangled MWCNT (including surface modified MWCNT). However, whether this concern is relevant for all or only some of the registered nanoforms of MWCNT cannot be resolved at present primarily due to the missing and comparative standard in vivo data.

Developmental toxicity

No guideline-conform developmental toxicity study was provided in the registration dossiers. The provided waiving arguments are considered invalid.

The only provided OECD TG 421 study with a registered material did not report any developmental effects. It is noted, however, that an OECD TG 421 does not provide adequate information on developmental toxicity.

Additional relevant data were identified in the scientific literature. Two studies testing for developmental effects of one specific registered MWCNT form when administered via IT instillation did not find evidence for developmental toxicity per se, but reported adverse effects of tested MWCNT on offsprings' immune responses (Hansen et al., 2014b; Hougaard et al., 2013).

Further studies testing other (non-registered) forms of tangled MWCNT with similar dimensions orally (Lim et al., 2011a; Lim et al., 2011b; Wang et al., 2014), via IT instillation (Hojo et al., 2018; Zhang et al., 2018) or via IP injection (Ivani et al., 2012) were identified in the scientific literature. While oral administration of pristine and surface-modified tangled MWCNT did not yield any developmental effects in mice, administration of such MWCNTs via IT and IP resulted in adverse effects in mouse offspring. Likewise, IV injection of COOH-MWCNT resulted in developmental toxicity (Huang et al., 2014; Qi et al., 2014). Additional in vitro studies further suggest a toxic potential of relevant MWCNT on developing organisms (Aminzadeh et al., 2017; Darne et al., 2014; Qu et al., 2017; Xu et al., 2016).

Taken together, the identified information shows that there is a concern for developmental toxicity of tangled MWCNT (including surface-modified forms). This concern, however, cannot be resolved at present due to missing standard data and the above mentioned characterisation issues.

7.9.8. Other effects

Cardiovascular system

The exposure of test animals, human cell lines or platelets showed that MWNCT are capable to interact or activate the cardiovascular system and cause adverse effects. It was observed that exposure to tangled MWCNT can result in platelet agglomeration, altered blood pressure and blood lipid composition, accelerate aortic plaque progression, arrhythmia, impair heart functions and increased cardia damage after ischemia and reperfusion. Available data in the scientific literature were mainly obtained after IT instillation. (Cao et al., 2014; Chen et al., 2015; Gaffney et al., 2015; Kim et al., 2015; Poulsen et al., 2015; Radomski et al., 2005; Thompson et al., 2014; Thompson et al., 2018; Xu et al., 2012).

The eMSCA noticed that IT instillation administers a bolus dose which can cause a local lung overdose and accompanied inflammation.

Neurologic system

Scientific literature showed that after IV injection MWCNT can be found in the central nervous system (CNS), crossing the blood-brain barrier (BBB). Corresponding studies indicate that MWCNT either directly or indirectly by inflammatory mediators, impair the BBB function. Observed amounts found in the CNS of exposed animals correspond to 0.4 – 3% of the initial dosage/g MWCNT (Costa et al., 2016; Kafa et al., 2016; Kafa et al., 2015; Wang et al., 2016). It was further observed that functionalised MWCNT and slightly thicker MWCNT (diameter ~36nm) are translocated at higher percentages/taken up more easily compared to thinner MWCNT (diameter ~10 nm) (Kafa et al., 2016; Shityakov et al., 2015). Once in the CNS, translocated MWCNT seem to mediate inflammatory responses via activation of mainly microglia cells and secondary astrocytes. Correspondingly, it was observed that regions rich in glia cells show stronger effects compared to regions with lower number of glia cells. Main localisation sides, studied in exposed animals and ex vivo experiments, addressed the hippocampal and thalamic region of the brain. In this brain regions MWCNT alter the electrophysiology as observed in rat hippocampus ex vivo, increased firing rate of pyramidal neurons or reduced opening number of voltage-gated potassium ion (K^+) channels. The eMSCA notes that it cannot be ruled out that the observed neuronal effects were related to possible impurities of the tested MWCNT. Removal of cobalt by annealing reduced the toxic potential of MWCNT (ex vivo) and induced glia cell transition into anti-inflammatory M2 phenotype whereas the pristine MWCNT did not. In addition, in vivo studies with (surface-modified) tangled MWCNT reported brain damage (necrosis) (Chen et al., 2013b) and behavioural changes in offspring (Ivani et al., 2012) after single IV injection of pregnant mice.

Immune system

Due to their extraordinary biodurability, MWCNT elicit a marked inflammatory foreign body response, activating and interacting with both, cells of the innate and the adaptive immune system. Phagocytosis by macrophages in the first line of defence responsible for clearance may be impaired by both overwhelming amounts of MWCNT and intracellular detrimental effects, the latter depending on structural and other physico-chemical MWCNT features. Retained MWCNT can then also interact with other recruited effector and regulatory cells of the immune system. Registrations included few studies investigating the adverse effects of two forms of MWCNT on immune cells, including macrophages and T lymphocyte cell lines as well as human peripheral blood mononuclear cells. For one registered MWCNT form, studies resulted in decreased cell viability, signs of oxidative stress, and altered differentiation potential (Di Cristo, 2012; Laverny et al., 2013). Considering a study from the scientific literature, MWCNT similar to the registered nanoforms caused immune modulating effects (Zhang et al., 2017a). However, there are also several studies – both, submitted in the registration and literature data – concluding that MWCNT do not affect the investigated immune cells (Palomaki et al., 2010; Thurnherr et al., 2011; Thurnherr et al., 2009). All in all, results are very inconsistent

and effects of MWCNT seem to depend on the form and specific physico-chemical properties (e.g. agglomeration, surface chemistry, functionalisation, and metal content). Therefore, a potential adverse effect cannot be excluded; however, this concern cannot be assessed at present, mainly due to a lack of standardised methodology.

Effects related to metallic impurities

The modulation of toxicity of MWCNT due to metallic impurities showed mixed results in the scientific literature. In general depletion of metal impurities seemed to reduce adverse effects. Metallic impurities related effects include enhanced inflammatory reactions due to increased oxidative stress (ROS generation via Fenton reaction), increased influx of PMN in lung, and increased number of lung tissue anomalies (from mild inflammation to extensive lesion formation) compared to purified MWCNT (Gernand and Casman, 2014; Meng et al., 2013; Vitkina et al., 2016)

The eMSCA notes that it cannot be ruled out that observed differences between purified MWCNT and MWCNT containing metal impurities were caused by alterations of the carbon structure of the MWCNT. To purify MWCNT washing with acids or annealing at high temperature can be performed, which can cause alterations of the MWCNT, i.e. add modifications or reduce structural defects that might have an impact on the toxicity. However, both purification techniques were reported to lead to reduced toxicity (metal depleted MWCNT) compared to metal containing MWCNT.

The eMSCA noted that some of the metallic impurities have harmonised classifications according to CLP, and due to the amount of contamination(s) reported in the registrations, these classification(s) would need to be applied to the respective MWCNT forms (see section 7.9.11).

7.9.9. Hazard assessment of physico-chemical properties

Structural features (e.g. lattice defects, surface functionalisation, etc.) and metallic contaminants affect the inherent oxidising potential of MWCNT (Gernand and Casman, 2014; Meng et al., 2013; Vitkina et al., 2016). Because the registered nanoforms markedly vary in these properties, there is a health concern regarding substance-related ROS generation, which in turn potentially triggers inflammation and mutagenicity, respectively. The provided information and justification(s) on the oxidising potential is deemed insufficient and cannot be extrapolated to all registered nanoforms.

7.9.10. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

The registrants have derived DNELs for workers based on local respiratory irritation, transient inflammation and absence of systemic effects following subchronic inhalation exposure, respectively. The eMSCA only partially agrees to the NOAECs used by the registrants for DNEL derivation (which show a marked variance between different test substances). Furthermore, read-across justification(s) of the test substances to other registered non-tested nanoforms is missing and insufficient, and respectively, data cannot be extrapolated due to incomplete characterisation, toxicokinetics, and toxicity data. The eMSCA concludes that the DNELs derived by the registrants potentially need further adjustment once additional information becomes available.

No DNELs for consumers have been derived by the registrants. By some registrants this was based on the argumentation that the exposure of consumers would not be applicable for the registered uses. Others considered the consumer exposure as negligible, when a release of the substance from the articles into which the substance has been incorporated is taken into account as an exposure source for consumers.

7.9.11. Conclusions of the human health hazard assessment and related classification and labelling

The available information is not sufficient to conclude on classification. The eMSCA notes that some of the registered forms of MWCNT contain metallic impurities, which are classified as e.g. STOT RE, reproductive toxicant, and/or respiratory/skin sensitiser according to the CLP Regulation. Thus, registered MWCNT containing such classified impurities to an equal or greater amount than the respective cut-off value(s) should be self-classified according to Article 11 of the CLP Regulation (ECHA 2017, Guidance on the application of CLP criteria, Version 5.0).

7.10. Assessment of endocrine disrupting (ED) properties

Not assessed.

7.11. PBT and vPvB assessment

Not assessed.

7.12. Exposure assessment

7.12.1. Human health

7.12.1.1. Worker

The Chemical Safety Assessments (CSA) for MWCNT, except the CSA from one registrant, concluded that the substance does not meet the criteria for classification as dangerous in accordance with Regulation (EC) No. 1272/2008 and is not considered to be a PBT or vPvB substance by the registrants. Additionally, no indication of any other concern was raised. Thus, these registrants considered that the Chemical Safety Assessment does not need to include an exposure assessment for the workplace.

Some registrants showed with their Chemical Safety Reports (CSR) that, using the exposure model ECETOC TRA, exposure to workers is very low. This is mainly due to the use of technical and organizational measures, like closed system operation or solid/liquid matrix bound use of the substance. These measures prevent the exposure via inhalation as the most likely route of exposure for the evaluated substance.

The eMSCA concludes that the available information on worker exposure indicates the potential exposure to be very low for some of the nanoforms, but is in general terms insufficient to conclude on the resulting exposure at the workplace for all nanoforms.

7.12.1.2. Consumer

The CSAs for MWCNT, except the CSA from one registrant, concluded that the substance does not meet the criteria for classification as dangerous in accordance with Regulation (EC) No. 1272/2008 and is not considered to be a PBT or vPvB substance by the registrants. In addition, the registrants considered no other concern to be indicated. In consequence these registrants considered that the Chemical Safety Assessment does not need to include an exposure assessment for consumers.

For consumers no direct use of the substance itself or of mixtures containing it has been registered. The use of the articles into which the substance has been included could result in consumer exposure, if free particles of the substance are released during the service life, e.g. by mechanical manipulation and/or matrix alterations over time. Some registrants have addressed and provided information on this potential exposure source in

their Chemical Safety Assessments (e.g. by referring to published studies as Bello et al. (2009).

Kovochich et al. (2018) have reviewed studies in publicly available literature characterising the release of carbon nanotubes (CNT) from nanocomposites. They concluded the data suggests that several matrix types are capable to release free or bundled CNT in combination with some of the employed stressors.

The eMSCA concludes that the currently available information on the applications of the substance and exposure is insufficient to conclude on the resulting consumer exposure. A low level consumer exposure will need to be taken into account to ensure precaution in the subsequent risk assessment and comparison with the outcome of the hazard assessment of the registered forms of the substance.

7.12.2. Environment

The CSAs for MWCNT, except the CSA from one registrant, concluded that the substance does not meet the criteria for classification as dangerous in accordance with Regulation (EC) No. 1272/2008 and is not considered to be a PBT or vPvB substance by the registrants. Additionally, no indication of any other concern was raised. Thus, these registrants considered that the Chemical Safety Assessment does not need to include an Exposure Assessment for the Environment.

One registrant showed with its own CSA that a qualitative CSA needs to be done due to the hazard potential and due to the yearly tonnage produced. It was concluded that release into the environment is considered to be negligible. The argument of the registrant is that the system for manufacturing is entirely closed and due to the dispersion into polymeric matrices, release is also minor.

However, available information is insufficient to allow the eMSCA to comprehend the reasoning of the registrant.

The eMSCA concludes that currently the available information on use, fate and behaviour is insufficient to conclude on the environmental exposure.

7.13. Risk characterisation

Workers

As explained above, the eMSCA concludes that currently the available information on exposure shows very low exposure for some of the nanoforms but it is in general terms insufficient to conclude on exposure at the workplace. Along with the insufficient information on hazard it is currently not possible to conclude on a workplace risk.

Consumers

As explained above, the eMSCA concludes that an adequate HH hazard assessment for the registered MWCNT is not possible. Moreover, the derivation of consumer DNELs by the eMSCA, which are representative for all forms registered, is currently not feasible.

The available information on the application of the substance and resulting consumer exposure is currently insufficient for the eMSCA to exclude consumer exposure. A low level consumer exposure will need to be taken into account to ensure precaution in the eMSCAs risk assessment. To be able to conclude on the significance of this potential exposure, a comparison with the outcome of the hazard assessment of the registered forms of the substance is necessary but currently not feasible.

Environment

As explained above, the eMSCA concludes that currently the available information on hazard and exposure is insufficient to conclude on environmental risk.

7.14. References

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