Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	Multi-Walled Carbon Nanotubes (MWCNT), synthetic graphite in tubular shape
Chemical Group:	
EC Number:	231-955-3 / 936-414-1
CAS Number:	7782-42-5 / -
Submitted by:	Germany
Date:	17/03/2015

Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

Contents

1 IDENTITY OF THE SUBSTANCE

1.1 *Other identifiers of the substance*

Table 1: Substance identity

EC name:	Multiwalled carbon nanotubes
IUPAC name:	Multi-Walled Carbon Nanotubes (MWCNT), synthetic graphite in tubular shape
Index number in Annex VI of the CLP Regulation	N/A
Molecular formula:	C
Molecular weight or molecular weight range:	ca. $7.0 \cdot 10^7$ g·mol^{-1}
Synonyms/Trade names:	For EC 231-955-3: GRAPHITIZED PETROLEUM COKE ARTIFICIAL GRAPHITE,SYNTHETIC GRAPHITE GRAPHITE

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:

-

1.2 Similar substances/grouping possibilities

-

2 CLASSIFICATION AND LABELLING

2.1 *Harmonised Classification in Annex VI of the CLP*

Substance EC 936-414-1 is not listed in Annex VI of the CLP regulation.

2.2 *Self classification*

- In the registration:

    1. None for EC 936-414-1
    2. MWCNT under EC 231-955-3:

Eye damage	H319
STOT SE 3	H335

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

For EC 231-955-3 (state/form: nanomaterial; IUPAC name: MWCNT):

STOT SE 3	H335 (resp.)
Aquatic Chronic 3	H412

For CAS 1034343-98-0 (state/form: nanomaterial; IUPAC name: Graphene):

STOT SE 3:	H335 (resp.)
Eye Irrit 2	H319

For Multi-Walled Carbon Nanotubes (MWCNT), synthetic graphite in tubular shape, EC No 936-414-1:

Not classified

There are numerous other notifications under this EC-number but further nanomaterials – though likely among records - could not be identified.

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

No proposal for harmonised classification is publically available.

3 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA dissemination site		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☒ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☒ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☒ Confidential

Largest tonnage band refers to the joint submission for EC 231-955-3/CAS 7782-42-5 (Graphite). For an individual submission for this EC-no. the tonnage is confidential.
The smaller tonnage refers to the registered substance EC 936-414-1.

There may be further information for MWCNT under the substances "activated carbon" (CAS 7440-44-0) and "graphene" (CAS 1034343-98-0).

☒ Industrial use	☒ Professional use	☒ Consumer use	☒ Closed System

MWCNTs have a wide spread use including a number of consumer uses. Consumer uses are expected to grow rapidly due to the superior material properties of the nanomaterial such as extreme hardness yet low weight, fibre tension, etc. These and the estimated world market are mentioned in the COMMISSION STAFF WORKING PAPER - Types and uses of nanomaterials, including safety aspects {COM(2012) 572 final}(http://ec.europa.eu/health/nanotechnology/docs/swd_2012_288_en.pdf):

"According to SRI, the market of carbon nanotubes (thinner than 20 nm) worldwide is estimated around 200-250 tonnes (€30-40 million, mostly multi-walled carbon nanotubes) in 2009. The largest use is as a product imparting electrical conductivity to plastic materials, e.g. in disk drive components or automotive plastic fuel lines and fenders (electrostatic coatings). Other uses include polymer additives, paints and coatings, fuel cells, electrodes, electrolytes and membranes in batteries, especially in miniature lithium batteries. There is a lot of research and development into new applications, including into "in-situ component use" which might in term complement and expand the use of silicon in electronics. Workplace exposure can occur at production, use, when machining materials and from waste and depends on the work procedure and applied risk management measures. Measurements of airborne CNTs in workplaces in research and industrial settings have shown a likely exposure of workers in some cases. Higher levels of airborne CNTs were found in particular where processes such as extrusion and cutting of bags containing nanomaterials, dry-sawing of nanomaterial-containing composites took place. Exposure to humans and the environment at the use stage is considered to be low because it is bound in a matrix in most uses. There are ongoing discussions whether release at the waste stage could lead to exposure to significant amounts of nanoparticles. Impacts on recycling are also under investigation."

4 OTHER COMPLETED/ONGOING REGULATORY PROCESSES THAT MAY AFFECT SUITABILITY FOR SUBSTANCE EVALUATION

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☒ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	
Registration data contains testing proposals for the following endpoints: 6.1.2 long-term toxicity fish.	

5 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1 Legal basis for the proposal

☐ Article 44(2) (refined prioritisation criteria for substance evaluation)

☒ Article 45(5) (Member State priority)

5.2 Selection criteria met (why *the substance qualifies for being in CoRAP)*

☒ Fulfils criteria as CMR/ Suspected CMR

☐ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☐ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☐ Fulfils exposure criteria

☒ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐C ☐M ☐R	Suspected CMR[1] ☒C ☐M ☐R	☐ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[1]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)
Exposure/risk based concerns		
☒ Wide dispersive use	☒ Consumer use	☐ Exposure of sensitive populations
☒ Exposure of environment	☒ Exposure of workers	☒ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

There is an initial concern regarding possible risks for consumers and workers for MWCNT.

There is a concern due to a discrepancy in self-classification for the two dossiers which requires clarification (H319: Causes serious eye irritation; H335: May cause respiratory irritation). As stated in the dossier for EC 936-414-1, toxicology of MWCNT strongly depends on PC properties and dimensions, allowing an evaluation on a case-by-case basis only. Clarification of the PC/toxicity equivalency is considered a major assignment in a substance evaluation for MWCNT.

(Nano-)specific concerns:

1. STOT-RE

EC 936-414-1:

The key 90 d RDT study for inhalation (Pauluhn, 2010) resulted in a LOAEC = 0.4 mg/m^3 (lung inflammation with persistent lesions in the respiratory tract), which would justify classification STOT-RE cat. 1 (< 0.02 mg/l). Another important study (Ma-Hock et al. 2009) identified granuloma already at 0.1 mg/m^3. However, the test material used in this study - though showing a similar morphology - was less pure, containing ca. 10% Al_2O_3.

EC 231-955-3:

An inhalation 90 d study is ongoing and its results will be included in the substance evaluation process.

Recent scientific studies demonstrated extrapulmonary transport and permanent fibrotic responses in mice after 12 d of inhalation exposure with 5 mg/cm^3 MWCNT of the fibre type (Mercer et al., 2013, 2013a).

[1] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

2. Carcinogenicity

There are basically two different forms of MWCNT commercially available: one with a more rigid, long-fibre (asbestos-like) morphology and another one with a more tangled, low-density agglomerate form. The above registrations specifically address the latter type. The former were shown to rapidly induce mesothelioma formation in experimental animal studies (Poland 2008, Takagi 2008, Sakamoto 2009). Single intraperitoneal exposure of entangled MWCNT did not produce significant mesothelioma in rats at 20 mg/m^3 24 months post-exposure (Nagai et al., 2013).
An adequate long-term inhalation study for the registered, tangled type of MWCNTs is not available.

3. Environment

Based on the differing intrinsic characteristics and properties of MWCNT the concern raises that significant effects on environmental organisms together with a rather unknown exposure might occur. Environmental exposure has to be expected since MWCNT are considered as persistent in the environment. Therefore, existing data within the dossiers on hand (mainly comprising acute aquatic tests) are not sufficient to properly assess potential hazards/risk of MWCNT.

5.4 Preliminary indication of information that may need to be requested to clarify the concern

☒ Information on toxicological properties	☒ Information on physico-chemical properties
☒ Information on fate and behaviour	☒ Information on exposure
☒ Information on ecotoxicological properties	☐ Information on uses
☐ Information ED potential	☐ Other (provide further details below)

Information on the effects in humans after chronic inhalation as well as information on the carcinogenic properties of MWCNT are currently missing. However, there are long-term studies to be finalized both after inhalation and intraperitoneal exposure with different forms of MWCNT[2]. Additionally, a chronic inhalation study (TG 452) or a combined chronic/carcinogenicity study (TG 453) might be required with a test material identical to the registered nanosubstances. Later on, in case classification for carcinogenicity is required, further information on exposure may be requested.

It is expected that updated information with regulatory impact becomes available soon, such as the MWCNT dossier submitted to the WPMN/OECD within the Sponsorship Programme for the Testing of Manufactured Nanomaterials (http://www.oecd.org/science/nanosafety/).

Regarding environmental assessment, a test strategy including additional chronic toxicity tests as well as terrestrial and sediment tests are essential to reliable evaluate the hazards of MWCNT. This testing strategy should include a proper reporting on the sample preparation, application of the sample into the test system as well as a thorough verification of the behaviour and fate of the sample in the test system.

The nanosubstance evaluation can make use of several legal regulations affecting MWCNTS already in force or under way in non-European countries, such as Australia, Japan, and the U.S.

[2] With respect to rigid fibres of WHO dimension, an inhalation study with experimental animals is not appropriate as the sensitivity of this model is known to be poor. Therefore, in order to investigate the carcinogenic property of this type of MWCNT, a study with intraperitoneal application would be needed (Wardenbach et al., 2005).

References:

Ma-Hock L, Treumann S, Strauss V, Brill S, Luizi F, Mertler M, Wiench K, Gamer AO, van Ravenzwaay B, Landsiedel R. (2009).Inhalation toxicity of multiwall carbon nanotubes in rats exposed for 3 months. Toxicological Sciences, 112, 468-81.

Mercer RR, Scabilloni JF, Hubbs AF, Battelli LA, McKinney W, Friend S, Wolfarth MG, Andrew M, Castranova V, Porter DW. (2013).Distribution and fibrotic response following inhalation exposure to multi-walled carbon nanotubes. Particle and Fibre Toxicology, 10.

Mercer RR, Scabilloni JF, Hubbs AF, Wang LY, Battelli LA, McKinney W, Castranova V, Porter DW. (2013).Extrapulmonary transport of MWCNT following inhalation exposure. Particle and Fibre Toxicology, 10.

Nagai H, Okazaki Y, Chew SH, Misawa N, Miyata Y, Shinohara H, Toyokuni S. Intraperitoneal administration of tangled multiwalled carbon nanotubes of 15 nm in diameter does not induce mesothelial carcinogenesis in rats. Pathol Int. 2013 Sep;63(9):457-62.

Pauluhn J. (2010).Subchronic 13-week inhalation exposure of rats to multiwalled carbon nanotubes: Toxic effects are determined by density of agglomerate structures, not fibrillar structures. Toxicological Sciences, 113, 226-42.

Wardenbach P, Rödelsperger K, Roller M, Muhle, H (2005). Classification of man-made vitreous fibers: Comments on the revaluation by an IARC working group. Regulatory Toxicology and Pharmacology, 43, 181-193

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
Possible harmonized classification for STOT RE and for carcinogenicity for a number or group of defined MWCNT nanomaterials and possible exemption of other nanoforms of the same substance as well as environmental classifications might be considered depending on the evaluation outcome.			