Committee for Risk Assessment

RAC

Annex 1

Background document

to the Opinion proposing harmonised classification and labelling at Community level of

Glass microfibres of representative composition

EC number: -

CAS number: -

CLH-O-0000001412-86-35/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

04 December 2014

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

Substance Name: glass fibres of representative composition [Calcium-aluminium-silicate fibres with random orientation with the following composition (% given by weight): SiO2 55.0-60.0%, Al2O3 4.0-7.0%, B2O3 8.0-11.0%, ZrO2 0.0-4.0%, Na2O 9.5-13.5%, K2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe2O3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F2 <1.0% with note R. Process: typically produced by flame attenuation and rotary process. (Additional individual elements may be present at low levels; the process list does not preclude innovation)]

EC Number: **Not assigned**

CAS Number: **Not assigned**

Index Number: **Not assigned**

Contact details for dossier submitter: ANSES (on behalf of the French MSCA)
253 avenue du General Leclerc
F-94701 Maisons-Alfort Cedex
+33 1 56 29 19 30
reach@anses.fr

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	glass fibres of representative composition [Calcium-aluminium-silicate fibres with random orientation with the following composition (% given by weight): SiO2 55.0-60.0%, Al2O3 4.0-7.0%, B2O3 8.0-11.0%, ZrO2 0.0-4.0%, Na2O 9.5-13.5%, K2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe2O3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F2 <1.0% with note R. Process: typically produced by flame attenuation and rotary process. (Additional individual elements may be present at low levels; the process list does not preclude innovation)]
EC number:	-
CAS number:	-
Annex VI Index number:	-[1]
Degree of purity:	100%
Impurities:	N/A for UVCB substance

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation	
Current entry in Annex VI, CLP Regulation		
Current proposal for consideration by RAC	Carc. 2 – H351 (with note R)*	
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Carc. 2 – H351 (with note R)*	

*** The text of the notes is given in section 2.1 of the CLH report.**

[1] Index numbers 650-016-00-2 and 650-017-00-8 in Annex VI of CLP are not applicable

1.3 Proposed harmonised classification and labelling based on CLP Regulation

Table 3: Proposed classification according to the CLP Regulation

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives	None		None	Not evaluated
2.2.	Flammable gases	None		None	Not evaluated
2.3.	Flammable aerosols	None		None	Not evaluated
2.4.	Oxidising gases	None		None	Not evaluated
2.5.	Gases under pressure	None		None	Not evaluated
2.6.	Flammable liquids	None		None	Not evaluated
2.7.	Flammable solids	None		None	Not evaluated
2.8.	Self-reactive substances and mixtures	None		None	Not evaluated
2.9.	Pyrophoric liquids	None		None	Not evaluated
2.10.	Pyrophoric solids	None		None	Not evaluated
2.11.	Self-heating substances and mixtures	None		None	Not evaluated
2.12.	Substances and mixtures which in contact with water emit flammable gases	None		None	Not evaluated
2.13.	Oxidising liquids	None		None	Not evaluated
2.14.	Oxidising solids	None		None	Not evaluated
2.15.	Organic peroxides	None		None	Not evaluated
2.16.	Substance and mixtures corrosive to metals	None		None	Not evaluated
3.1.	Acute toxicity - oral	None		None	Not evaluated
	Acute toxicity - dermal	None		None	Not evaluated
	Acute toxicity - inhalation	None		None	Not evaluated
3.2.	Skin corrosion / irritation	None		None	Not evaluated
3.3.	Serious eye damage / eye irritation	None		None	Not evaluated
3.4.	Respiratory sensitisation	None		None	Not evaluated
3.4.	Skin sensitisation	None		None	Not evaluated
3.5.	Germ cell mutagenicity	None		None	Not evaluated
3.6.	Carcinogenicity	Carc. 2 – H351		Carc. 2 – H351	
3.7.	Reproductive toxicity	None		None	Not evaluated
3.8.	Specific target organ toxicity –single exposure	None		None	Not evaluated
3.9.	Specific target organ toxicity	None		None	Not evaluated

	– repeated exposure				
3.10.	Aspiration hazard	None		None	Not evaluated
4.1.	Hazardous to the aquatic environment	None		None	Not evaluated
5.1.	Hazardous to the ozone layer	None		None	Not evaluated

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Signal word: "Warning"
Hazard statements: H351
Precautionary statements: not harmonised
Pictogram: GHS08

Proposed notes assigned to an entry: Note R. The text of the note is detailed in section 2.1 of the CLH report.

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

In annex VI of Regulation 1272/2008 (CLP), fibres with a harmonised classification (C&L) are man-made vitreous fibres (MMVF) which are subdivided in two different entries (see table below). The two entries 650-016-00-2 and 650-017-00-8 refer to "mineral wool" and "refractory ceramic fibres" (RCFs) respectively. These entries are differentiated by their name and their chemical composition with respect to the content of alkali/alkali earth metal oxides with 18 % being the cut-off point. Their hazardous properties and C&L according to CLP also vary from 'suspected carcinogen to humans' (Carc. 2, entry 650-016-00-2) to 'presumed to have carcinogenic potential for humans' (Carc. 1B, entry 650-017-00-8).

Although "special purpose fibres" are explicitly mentioned in the phrasing of the current Refractory Ceramic Fibres entry (index number 650-017-00-8), the appropriate entry for '475' type glass fibres regarding the alkaline oxide and alkaline earth oxide content (K_{NB} index) should be for "Mineral wool". This discrepancy in the identification of the appropriate entry for '475' type glass fibres requires a new specific entry.

Index number	**Substance Name**	**Classification**	**Nota**
650-016-00-2	Mineral wool, with the exception of those specified elsewhere in this Annex; [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide ($Na_2O+K_2O+CaO+MgO+BaO$) content **greater than 18 %** by weight]	Carc. 2 – H351	A, Q, R
650-017-00-8	Refractory Ceramic Fibres; **Special Purpose Fibres**, with the exception of those specified elsewhere in this Annex; [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide ($Na_2O+K_2O+CaO+$ MgO+BaO) content less or equal to 18 % by weight]	Carc. 1B – H350i	A, R

In its evaluation, IARC (2002) concluded that special-purpose glass fibres such as E-glass and '475' glass fibres are possibly carcinogenic to humans (Group 2B). In addition, IARC reported that current average exposure levels to MMVF are generally less than 0.5 respirable fibre/cm^3 (500 000 respirable fibres/m^3) as an 8-h time-weighted average but that higher levels have been measured in production of special-purpose glass fibres, increasing the concern for workers.

In November 2005, a French proposal was submitted at the TC C&L for a classification of special purpose fibres 'E' and '475' as Carc. Cat.2; R45 (Carc. 1B under CLP). However, in October 2006, the TC C&L agreed to classify 'Type 475 Special purpose fibres' with Carc. Cat. 3; R40 (currently

Carc. 2 under CLP) and 'E-glass fibres' with Carc. Cat. 2; R49 (currently Carc. 1B under CLP) (Follow-up III of TC C&L October 2006; doc ECBI/09/07). Indeed, largely based on animal evidence, E-glass fibres are presumed to have carcinogenic potential for humans whereas type '475' glass fibres are suspected to be human carcinogens. TC C&L discussions (2005, 2006) are added in annex of this dossier. This decision was however not included in an ATP before the entry into force of CLP (2008).

In March 2013, a French proposal for classification was submitted on type '475' special purpose fibres to ECHA followed by a public consultation (PC) from 5 March 2013 until 19 April 2013. During PC, a number of issues were raised by a manufacturer including the use of the '475' which is a commercial name of Johns Manville (JM) product (e.g. JM475) and the incorrect composition and manufacturing process. An additional literature reference was also submitted (Bernstein, 2007) in which typical ranges of composition of type '475' special-purpose glass fibres were given, including for other commercial names (e.g. Evanite B and Laucher B-glass). In addition, the manufacturer proposed an alternative name for the substance specifying the use ('filtration') and the manufacturing process. Comments were also received on the registration status of fibres of this kind which have been registered under registration number 01-2119615609-34-XXXX.

In January 2014, the French proposal was withdrawn. It was acknowledged that type '475' is the commercial name of a product by JM. In addition, fibres of the type where '475' is considered as a representative example are rather unique among the family of synthetic mineral fibres due to their chemical composition and physical characteristics (Hutten, 2007). They are used not for general insulation but for "high-end" filtration products designed for high and ultra-high purity filtration of air and liquids. The designation for these types of filters varies with country and includes HEPA, ULPA, EU 10-13, EN1822, and S3 (IARC, 2002). A specific glass composition manufactured to have typically a diameter < 3μm is known in the industry literature as glass of type '475' formulation. Glass fibres of this type are considered "special purpose" as they are specifically manufactured to have a diameter generally < 3μm and are not used as general insulation fibres.

Type 475 fibres manufactured by JM are coded according to a mean fibre diameter, with larger number indicating larger diameters (e.g. JM 110/475 fibres have a greater nominal diameter (1.9-3.0 μm) than JM 100/475 fibres (0.28-0.38 μm). In technical literature, the fibres of this type are referred to as '475' as it is the most widely tested brand of this type of glass fibres. Evidently, different manufacturers will have their own commercial names for fibres with this glass formulation and physical characteristics. According to Johns Manville website (2014), the diameter for type '475' can be as large as 5 μm.

Regarding the manufacturing process, special purpose glass fibres of this type are usually produced with a flame attenuation or rotary fiberisation process, which results in the production of very small diameter fibres (IARC, 2002; Pico et al, 2012, Hutten 2007).

Justification for the proposal of a new specific entry:

For the reasons described above, it is therefore proposed to clarify the scope of the original entry to cover glass fibres of type '475'.

it is proposed to create a new entry in Annex VI of CLP for 'glass fibres of representative composition' (composition as given in the name), i.e.,

a representative alkaline/alkaline earth concentration ranges.

They are proposed to be classified as Carc. 2 with the hazard statement H351 and to be assigned with the note R (see below). The following naming of the new specific entry, arising from the

Follow-up III of TC C&L October 2006 (doc ECBI/09/07), registration dossiers and comments received during PC:

'**glass fibres of representative composition [Calcium-aluminium-silicate fibres with random orientation with the following composition (% given by weight): SiO2 55.0-60.0%, Al2O3 4.0-7.0%, B2O3 8.0-11.0%, ZrO2 0.0-4.0%, Na2O 9.5-13.5%, K2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe2O3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F2 <1.0% with note R. Process: typically produced by flame attenuation and rotary process. (Additional individual elements may be present at low levels; the process list does not preclude innovation)].**'

Proposal of notes:

The notes A and Q are not proposed for the specific entry of these glass fibres.

Note A applies in order to give the exact name of the substance on the label and not the name of the entry in the cases of generic entries. The new entry proposed is not a generic entry and note A is therefore not relevant.

Note Q applies for the general entry for fibres (index 650-016-00-2) to be able to distinguish fibres that are of less concern and should be exempted from the carcinogenic classification. The available data as shown in this dossier demonstrate the carcinogenic potential of type '475' glass fibres and it is not relevant to include exemption conditions in this new entry.

The note R is proposed for this new specific entry. The note R applies for the fibres with a length weighted geometric mean diameter inferior to 6 µm.

Text of notes (CLP Regulation):

A: Without prejudice to Article 17(2), the name of the substance must appear on the label in the form of one of the designations given in Part 3. In Part 3, use is sometimes made of a general description such as "... compounds" or "... salts". In this case, the supplier is required to state on the label the correct name, due account being taken of section 1.1.1.4.

Q: The classification as a carcinogen need not to apply if it can be shown that the substance fulfils one of the following conditions:

- a short term biopersistence test by inhalation has shown that the fibres longer than 20 µm have a weighted half-life less than 10 days; or
- a short term biopersistence test by intratracheal instillation has shown that the fibres longer than 20 µm have a weighted half-life less than 40 days; or
- an appropriate intra-peritoneal test has shown no evidence of excess carcinogenicity; or
- absence of relevant pathogenicity or neoplastic changes in a suitable long term inhalation test.

R: carcinogenic classification need not to apply to fibres with a length weighted geometric mean diameter – 2 standard geometric errors > 6 µm.

2.2 Short summary of the scientific justification for the CLH proposal

In its evaluation, IARC (2002) concluded that special-purpose glass fibres such as E-glass and '475' glass fibres[2] are possibly carcinogenic to humans (group 2B). In addition, IARC reported that current average exposure levels to MMVF are generally less than 0.5 respirable fibre/cm^3 (500 000 respirable fibres/m^3) as an 8-h time-weighted average but that higher levels have been measured in production of special-purpose glass fibres, increasing the concern for workers. Nevertheless, carcinogenic differences seem to exist between type '475' and E-glass fibres (Bernstein, 2007).

Experimental data for type '475'glass fibres clearly provide evidence of a carcinogenic effect in several species (rats, hamsters and monkeys) and in both sexes in numerous independent studies in different laboratories. Tumours consist in both benign and malignant lung tumours (carcinomas, mesotheliomas and sarcomas) and abdominal tumours by different routes of exposure (inhalation, intraperitoneal, intratracheal and intrapleural). Indeed, special-purpose fibres show a carcinogenic potential by the intraperitoneal, intratracheal and intrapleural routes. Fibre biopersistency may enable their migration further inhalation into the pleural cavity and emphasise the relevance of positive results by the intrapleural route.

No study clearly demonstrates the induction of tumour following inhalation of glass fibres of '475' type and most of the available studies show important limitations. The epidemiological data do not bring sufficient evidence of carcinogenicity in human. Fibre biopersistency may enable their migration further inhalation into the pleural cavity and emphasise the relevance of positive results by e.g. the intrapleural route.

Overall, it is concluded that glass fibres of representative composition, as specified in the name (which includes type '475' and other special purpose glass fibres) are suspected to be human carcinogens and should be classified as Carc. 2 (H351) under the CLP Regulation.

2.3 Current harmonised classification and labelling

Not applicable.

2.4 Current self-classification and labelling

According to the comments received during public consultation of '475 special purpose glass fibres' subsequently withdrawn by France, type '475' glass fibres have been registered under REACH using the list number 924-055-3 using the chemical name 'Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content greater than 18 % by weight'. The classification registered is Carc. 2 (H351).

[2] Type "475" fibres refer to a specific type of glass fibres in terms of composition and physical characteristics (length, diameter) of which the product of the brand "475" is considered representative. In this report "475" is used as an example of this type of fibres as many of the experimental studies on which the classification is proposed used this particular brand of fibres. It does not single out this particular brand and fibres of this type have different brand names depending on the manufacturer. (Irwin M. Hutten. Handbook of Nonwoven Filter Media, 13 Feb 2007. Elsevier Science, ISBN: 978-1-85617-441-1)

For information, other fibres have also been registered using various chemical identifiers as shown in the table below (ECHA dissemination database accessed on 10 February 2014).

Information given in the registration dossier	CAS Number	EC/ListNumber	Proposed C&L	Registration No	Notifications in the C&L inventory
Glass, oxide, chemicals	65997-17-3	266-046-0	Carc. 1B, H350i	01-2119488048-29-XXXX	yes
No name given (Not technically possible following IUPAC rules) *Description: Refractories, alumino-silicate, fibres* Relates to alumino-silicate wools (ASW)	142844-00-6	604-314-4	Carc. 1B, H350	01-2119458050-50-XXXX	Yes (CAS only)
No name given (Not technically possible following IUPAC rules) *Description: Synthetic fibers, alk. earth silicate* Relates to alkaline-earth silicate (AES) fibres	436083-99-7	610-130-5	NC (note Q)	01-2119457644-32-XXXX	Yes (CAS only)
No name given (Not technically possible following IUPAC rules) *Description: Aluminium chloride, basic, reaction products with silica*	675106-31-7	614-074-2	NC	01-2119456884-25-XXXX	No
Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content greater than 18 % by weight	-	924-055-3	Carc. 2, H351	01-2119615609-34-XXXX	No
No name given (No IUPAC name allocated) *Description: Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+MgO+BaO) content greater than 18% by weight and fulfilling one of the note Q conditions* Relates to high alumina, low silica stone wools (HT wools)	-	926-099-9	NC (note Q)	01-2119472313-44-XXXX	No
Amorphous glass product formed from the melting and fiberisation of dipotassium oxide, oxo(oxo-alumanyloxy) alumane and dioxosilane Potassium alumino silicate glass fibre	675106-31-7	931-219-8	NC (note Q)	01-2119962882-26-XXXX	No

NC, not classified

An overview of fibres notified in the C&L inventory (accessed on 10/02/2014) is presented in the table below. For some of these entries, the classification varies from ‘not classified’ to ‘Carc. 1B’. The list number 924-055-3 using the name ‘Man-made vitreous (silicate) fibres with random

orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content greater than 18 % by weight' has not been used by notifiers.

Index Number	EC/list Number	CAS Number	Name	Overview of Notifications of classification according to CLP
650-016-00-2	-	-	Mineral wool, with the exception of those specified elsewhere in this Annex [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+MgO+BaO) content greater than 18 % by weight]	None [CLP: Carc. 2 (H351) (with notes R, Q and A)]
650-017-00-8	-	-	Refractory Ceramic Fibres, Special Purpose Fibres, with the exception of those specified elsewhere in this Annex [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content less or equal to 18 % by weight]	None [CLP: Carc. 1B (H350i) (with notes R and A)]
-	-	142844-00-6	Aluminosilicate (ceramic) fiber Aluminosilicate refractory ceramic fibres Refractories, fibers, aluminosilicate not technically possible following IUPAC rules	Carc. 1B (H350) with or without notes (70 notifications)
-	-	436083-99-7	Alkaline Earth Silicate Fibres	NC or Carc. 2 (H351) with or without notes (25 notifications)
-	-	-	Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content greater than 18 % by weight Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) content greater than 18 % by weight	Carc. 2 (H351) with or without notes (2 notifications)
-	-	-	Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+MgO+BaO) content greater than 18 % by weight No IUPAC name assigned	Carc. 2 (H351) with or without notes (11 notifications)
-	-	-	Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+ MgO+BaO) Reaction mass of aluminium oxide and silicon dioxide	NC or Carc. 1B (H350) with or without notes (5 notifications)
-	-	-	Aluminosilicate Refractory Ceramic Fibres	Carc. 1B (H350) with notes R & A (2 notifications)
-	-	-	Zirconia Aluminosilicate Refractory Ceramic Fibres	Carc. 1B (H350) with notes R & A (1

				notification)
-	266-046-0	65997-17-3	glass, oxide, chemicals (other names include fiberglass),	NC to Carc. 1B (H350) with no note (> 500 notifications)

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Glass fibres of the specific type (i.e. regarding their chemical composition and physical characteristics of which the commercial brand ‘475’ is considered to be representative) have CMR properties, i.e. carcinogenic property, that justifies a harmonised classification and labelling according to article 36 of CLP.

Considering the recommendations of IARC (2002), TC C&L (2006) and the REACH registration dossier (registration number 01-2119615609-34-XXXX), harmonisation of classification is considered to be required for this endpoint (carcinogenicity).

Part B.

SCIENTIFIC EVALUATION OF THE DATA

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 4: Substance identity

EC number:	-
EC name:	-
CAS number (EC inventory):	-
CAS number:	-
CAS name:	-
Name(s) in the IUPAC nomenclature or other international chemical name(s)	glass fibres of representative composition [Calcium-aluminium-silicate fibres with random orientation with the following composition (% given by weight): SiO2 55.0-60.0%, Al2O3 4.0-7.0%, B2O3 8.0-11.0%, ZrO2 0.0-4.0%, Na2O 9.5-13.5%, K2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe2O3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F2 <1.0% with note R. Process: typically produced by flame attenuation and rotary process. (Additional individual elements may be present at low levels; the process list does not preclude innovation)]
CLP Annex VI Index number:	[3]
Molecular formula:	Not applicable (a generic molecular formula cannot be provided for glass fibres as it is a UVCB substance)
Molecular weight range:	Not applicable

Structural formula: Not applicable

1.2 Composition of the substance

Table 5: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
Glass fibres	Ca 100%	-	-

Table 6: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks
None	-	-	-

Table 7: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
None	-	-	-	-

[3] Index numbers 650-016-00-2 and 650-017-00-8 in Annex VI of CLP are not applicable

1.2.1 Composition of test material

Not relevant.

1.3 Physico-chemical properties

Table 8: Summary of physico-chemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
State of the substance at 20°C and 101,3 kPa	Inorganic, solid, white odourless fibrous glass in bulk or blanket form	ATSDR, 2004	measured
Melting/freezing point	> 650°C	ATSDR, 2004	estimated
Boiling point	Not applicable		
Relative density	2.6 g/cm³ at 20°C	AFSSET, 2007	measured
Softening point	850 °C	AFSSET, 2007	measured
Maximal temperature of use	600 °C	AFSSET, 2007	measured
Devitrification temperature	800 °C	AFSSET, 2007	measured
Not fibrous particles or shot	minimal	AFSSET, 2007	measured
Refractive index	1.55	AFSSET, 2007	measured
Vapour pressure	Not applicable		
Surface tension	Not applicable		
Water solubility	Not soluble in water	ATSDR, 2004	measured
Partition coefficient n-octanol/water	Not applicable		
Flash point	Not applicable		
Flammability	Not applicable		
Explosive properties	Not applicable		
Self-ignition temperature	Not applicable		
Oxidising properties	Not applicable		
Granulometry	aerodynamic diameters corresponding to the fibre density, diameter and length < 4 um	Cullen, 2000	measured
Stability in organic solvents and identity of relevant degradation products	Not applicable		
Dissociation constant	Not applicable		
Viscosity	Not applicable		

RAC general comment

In annex VI of Regulation 1272/2008 (CLP), fibres with a harmonised classification are man-made vitreous fibres (MMVF) which are subdivided into two different entries (see table below).

Index No	International Chemical Identification	Hazard Class and Category Code(s)	Hazard statement Code(s)	Nota
650-016-00-2	Mineral wool, with the exception of those specified elsewhere in this Annex; [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na_2O +K_2O+CaO+MgO+BaO) content greater than 18 % by weight]	Carc. 2	H351	A, Q, R
650-017-00-8	Refractory Ceramic Fibres, Special Purpose Fibres, with the exception of those specified elsewhere in this Annex; [Man-made vitreous (silicate) fibres with random orientation with alkaline oxide and alkali earth oxide (Na_2O+K_2O+CaO+MgO+BaO) content less or equal to 18 % by weight]	Carc. 1B	H350i	A, R

The two existing entries in the CLP Regulation with index numbers 650-016-00-2 and 650-017-00-8 cover 'mineral wool' and 'Refractory Ceramic Fibres, Special Purpose Fibres', respectively. These entries are differentiated by name and the chemical composition with respect to the content of alkaline oxides and alkali earth metal oxides with 18 % by weight being the cut-off point. Their hazardous properties and harmonised classifications (CLH) also vary from 'suspected human carcinogens' (Carc. 2) to 'presumed human carcinogens' (Carc. 1B), respectively.

The CLH proposal originally submitted by the Dossier Submitter (DS) refers to glass fibres within the glass wool category and therefore continuous filaments are not within scope of the proposal. In addition, a new entry in Annex VI needs to be created for these glass microfibres of representative composition. This class of glass wool fibres consists of fine glass fibres forming a mass resembling wool; individual fibres are defined as being over 5 µm long and having a length-to-width (aspect) ratio of at least 3:1 (i.e., the fibre is at least three times as long as its width). There is considerable variation in the physico-chemical properties of individual fibres within this class, depending on the manufacturing process and end use. It is well-known that relatively small changes in composition can result in significant changes in the optical and electrical properties of the glass fibres. For example C-glass fibres are resistant to chemical attack, S-glass fibres have a high strength whereas E-glass fibres are poor conductors of electricity. A specific glass wool product often contains fibres with a wide range of diameters, as a result of the manufacturing process.

The manufacturing process also determines the particle length and diameter of the fibres. The methods of manufacture determine whether a fibre is a "General Purpose Fibre" or a "Special Purpose Fibre". "Special Purpose Fibres" are characterised by having a diameter

< 5µm while "General Purpose Fibres" are having a diameter > 5µm. A fibre of a given chemical composition can be either a "Special Purpose Fibre" or a "General Purpose Fibre" depending on the method of manufacture (E-glass fibres for example can be either general purpose insulation fibres or special purpose fibres). Special purpose fibres are referred to in this report as "microfibres" as this terminology is used in industry and is more representative than "special purpose". The typical process to produce the glass microfibres of representative composition is by flame attenuation and rotary process.

It is noted that a specific glass composition manufactured to have typically a diameter < 3 µm is known in the industry literature as grade or type '475'. Type '475' is a commercial name from one manufacturer and there are many commercial fibres that have the same composition and characteristics (diameter/length). As it was one of the most commonly tested glass fibre types, many literature reports refer to type '475' and 'special purpose' glass fibres. According to Bernstein (2007), type '475' microfibres are produced in many different diameters based on customer needs, but the most commonly sold products have mean diameters between 0.65 µm and 2.7 µm. According to Bernstein (2007), comparable microfibres other than grade or type '475' includes those with trade names 'Evanite B' and 'Laucher B-glass'.

For cancer hazard identification, it is important that fibres are classified according to their biological activity, including their biopersistence *in vivo* (Bernstein, 2007). The glass microfibres considered in this document with respect to the contents of alkaline oxides and alkali earth metal oxides as described in Annex VI of CLP (Na_2O +K_2O+CaO+MgO+BaO) being 13.5 – 30.5% by weight, have a mean content which is spread over the current 18% cut-off as described in existing Annex VI entries for fibres. Glass microfibres have a higher alkaline oxides and alkali earth metal oxides content than E-glass fibres of representative composition and also a lower content of Al_2O_3 (Campopiano *et al*., 2014).

Recognising the differentiation of biological effects of various types of glass fibres France submitted a proposal for the harmonised classification of glass microfibers. During the first public consultation (PC) of the CLH report (5 March to 19 April 2013), a number of issues were raised by manufacturers and downstream users (M/DU) including the incorrect composition and manufacturing process details. In addition, '475' was considered as a proprietary name to a M/DU. In November 2013, the French proposal was withdrawn. In February 2014, a new CLH dossier was submitted to ECHA on 'glass fibres of representative composition with SiO_2 55.0-60.0%, Al_2O_3 4.0-7.0%, B_2O_3 8.0-11.0%, ZrO_2 0.0-4.0%, Na_2O 9.5-13.5%, K_2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe_2O_3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F_2 <1.0%' followed by a PC from 5 March to 22 April 2014. After PC, the DS agreed to rename 'fibres' as 'microfibres' to distinguish between respirable 'glass microfibres' and 'glass Continuous Filament Glass Fibres' which are not respirable.

2 MANUFACTURE AND USES

2.1 Manufacture

Several European manufacturing sites produce articles and mineral wool products.

2.2 Identified uses

Industrial: air and liquid filtration (ASHRAE, HEPA, ULPA filter) in automotive applications and electronic industry (clean room filter), separation (battery) and insulation in aeronautical applications.

General public: In the filtration of high-efficiency air, the major application is the general ventilation of buildings (offices, schools, airports, hotels, department stores, residences, conference center). Otherwise, the domestic applications of special purpose fibres are filters for vacuum cleaners and the purifiers of air.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Not evaluated in this dossier**.**

4 HUMAN HEALTH HAZARD ASSESSMENT

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

No data.

4.2 Acute toxicity

No data.

4.3 Irritation

4.3.1 Skin irritation

Discussions took place on this endpoint at the TC C&L, leading to the conclusion that the classification for the skin irritation is not necessary.

No classification proposed.

4.4 Corrosivity

No data.

4.5 Sensitisation

No data.

4.6 Repeated dose toxicity (including biopersistency):

This endpoint is presented only for information and is not proposed for harmonised classification.

4.6.1 Non-human information

4.6.1.1 Repeated dose toxicity: oral

No data.

4.6.1.2 Repeated dose toxicity: inhalation

Species	Fibre type	Conc.			Expo. time (h/day)	Duration	Observations and Remarks	Ref.
		Total	WHO	L>20 µm				
Wistar rats (n=3 / group)	100/475 (475)	912 f/cm^3			-	7 h	<u>'475' type -glass fibres:</u> • No increase in cell proliferation as measured by BRDU uptake (increase with amosite)	Donald-son 1995
Male Fischer rats (n=74 / group)	MMVF32(E)	38±9 mg/m^3	316±50 f/cm^3	146±28 f/cm^3	6h/d nose-only	5 days + 1 year recovery	<u>E-glass fibres:</u> • Geometric mean dimension: length: 16.1±2.4 µm, diameter: 0.81±1.98 µm • Weighted half-time of fibres longer than **20 µm**: **79 days** (95% CI: 62-96) • 90% clearance of fibres longer than **20 µm**: **371 days** (95% CI: 272-506) • k_{dis} = 11 ng/cm^2/h	Hester-berg 1998 (Eastes 2000)
	MMVF33 (475)	36±8 mg/m^3	371±55 f/cm^3	163±25 f/cm^3			<u>475-glass fibres:</u> • Geometric men dimension: length: 16.2±2.3 µm, diameter: 0.74±2.20 µm • Weighted half-time of fibres longer than **20 µm**: **49 days** (95% CI: 40-58) • 90% clearance of fibres longer than **20 µm**: **240 days** (95% CI: 195-300) • k_{dis} = 17 ng/cm^2/h	

4.6.1.3 Repeated dose toxicity: dermal

No data.

4.6.1.4 Repeated dose toxicity: other routes

Intra-peritoneal:

Species	Fibre type	Dose			Injection schedule	Duration of observation	Observations and Remarks	Ref.
		Total	WHO	L>20 µm				
Male C57/B16 mice (n=3 or 4)	100/475 (475)	-	8.2 x 10^7 f	-	1 x 0.5 ml saline	4 days	• Marked increase in the number of inflammatory cells in the peritoneal cavity 4 days after injection: 14.0 compared to 1.6 million macrophages in control group and 4.58 compared to 0.04 millions of granulocytes in control group.	Davis 1996

Intra-tracheal:

	Fibre type	Dose	Duration of observation	Observations and Remarks	Ref.
Male Wistar rats (n=16)	100/475 (475)	1 x 1 mg	Lung analysis 3 days and 1 year after injection	• Persistence of fibres in the lung: Lung burden (million f. per lung) Fibre length 0.4<l<5 µm 5<l<20µm l>20µm 3 days 2236.8 221.3 8.4 12 mo. 182.4 69.7 2.7 • 1-year clearance of respectively 92, 68 and 68% compared with 96, 84 and 4% for amosite	Davis 1996 Searl 1999

4.6.1.5 Human information

No data.

4.6.1.6 Other relevant information

No data.

4.6.1.7 Summary and discussion of repeated dose toxicity

This endpoint is presented only for information and is not proposed for harmonised classification.

4.6.1.8 Summary and discussion of repeated dose toxicity findings relevant for classification according to DSD

This endpoint is presented only for information and is not proposed for harmonised classification.

4.6.1.9 Comparison with criteria of repeated dose toxicity findings relevant for classification according to DSD

This endpoint is presented only for information and is not proposed for harmonised classification.

4.6.1.10 Conclusions on classification and labelling of repeated dose toxicity findings relevant for classification according to DSD

This endpoint is presented only for information and is not proposed for harmonised classification.

4.7 Specific target organ toxicity (CLP Regulation) – repeated exposure (STOT RE)

No data.

4.8 Germ cell mutagenicity (Mutagenicity)

This endpoint is presented only for information and is not proposed for harmonised classification.

4.8.1 Non-human information

4.8.1.1 *In vitro* data

Test	Fibre type	Cell system	Protocol	Conc. (mg/l	Observations and Remarks	Ref.
Transfor-mation	JM100 (type 475)	BALB/c-3T3 cells	72 h	0-1-4-10-38-100 µg/cm^2	• Cytotoxicity at high concentration: around 30% of relative cloning efficiency at 10 µg/cm^2 • Dose-related transformation, significant from 10 µg/cm^2 • Transformed cells exerted anchorage-independent growth (90%)	Gao 1995
Transfor-mation	Code 100 (type 475)	Syrian hamster embryo cells	-	0.5 µg/cm^2 and above.	• Induction of cell transformation. • Milling of the fibres strongly reduced the effect.	Hester-berg 1984 and 1986
Transfor-mation	Code 100 (type 475) Code 110 (type 475)	Syrian hamster embryo cells		0-0.5-0.2-1.5 µg/cm^2 0-3-5-10-20 µg/cm^2	• Statistically significant increase in the transformation frequency at 1.5 µg/cm^2 with code 100 fibre (1.15 µg/cm^2 of fibres results in 1% transformed cell colonies and 62% of survival) • Slight, but not statistically significant or dose-dependent, increase in the transformation frequency with code 110 fibre (larger diameter than code 100).	Mikalse n 1988

Transformation	JM 104/475 (type 475)	Syrian hamster embryo cells (M3E3/C3)		0-50-100-150 µg/ml	• Significant decrease in cell survival (around 45% of surviving cell at 50 µg/ml and less than 10% at highest doses. • No effect of transformation • Microscopic observation: break of the filamentous structure of the actin system into a granular configuration; complete depolymerisation of the filamentous tubulin system.	Aufderheide 1994
Micronucleus	Code 100 (type 475)	Syrian hamster embryo cells	-	1 µg/cm^2	• Induction of micronuclei • Milling of the fibres strongly reduced the effect.	Hesterberg 1986
Chromosomal aberrations	Code 100, 104, 108A, 108B (type 475)	Chinese hamster lung cells		Up to 300 µg/ml	• Fibre samples were crushed and 90% of fibres were < 5 µm long. • Inhibition of colony formation: TD_{50} of 10, 11, 18 and 27 µg/ml, respectively. • No induction of chromosomal aberrations but polyploidy from 10 µg/ml with code 100 and 104 et 100 µg/ml with 108A	Koshi 1991
Micronucleus	Type 475 fibres of various diameters (code 90, 108, 110, 112)	Chinese hamster ovarian cells	48 h	Approx. 25 to 150 x10^4 f/cm^2	• Increased incidence of morphologically abnormal nuclei with little or no loss of viability • Concentration-dependent decrease in proliferation • No significant influence of diameter on toxicity when concentration are expressed as number of fifres/cm²	Hart 1994
Micronucleus	JM100 (475)	Chinese hamster lung fibroblast cell line (V79 cells)	24 h	0-10-20-40-80 µg/ml	• Dose-related increase of micronucleated (6.8% at 80 µg/ml) and multinucleated (49.5% at 80 µg/ml) cells. • Significant increase in kinetochore positive micronuclei in cells.	Ong 1997

4.8.1.2 In vivo data

No data.

4.8.2 Human information

No data.

4.8.3 Other relevant information

No data.

4.8.4 Summary and discussion of mutagenicity

This endpoint is presented only for information and is not proposed for harmonised classification.

4.8.5 Comparison with criteria

This endpoint is presented only for information and is not proposed for harmonised classification.

4.8.6 Conclusions on classification and labelling

This endpoint is presented only for information and is not proposed for harmonised classification.

No classification is proposed.

4.9 Carcinogenicity

4.9.1 Non-human information

4.9.1.1 Carcinogenicity: oral

No data.

4.9.1.2 Carcinogenicity: inhalation

Species	**Fibre: type 475**	Conc. Total	Conc. WHO	Conc. L>20 µm	Expo. Time (h/day)	Duration	Observations and Remarks	Ref.
AH/HAN rats (n=38)	100/475 (type 475)	5.8 mg/m^3 (estimated)	1119 f/cm^3	137 f/cm^3	7h/d 5d/wk whole-body	12 months lifetime obs.	• After 14 days of exposure: no increase in macrophage and neutrophil levels in the BALF, no increase in cell proliferation at different lung levels but increased level of LDH after 1, 3, 7 or 14 days of exposure. • Raised macrophage number at the end of exposure • No significant lung fibrosis reported (11 animals with very slight fibrosis) • 4 rats (11%) developed benign pulmonary neoplasms. None developed carcinoma nor mesothelioma. • In the control group (n=38), 1 rat (2.6%) developed a pulmonary adenoma and 1 rat a carcinoma. • In the amosite group (n=42), 16 rats (38%) developed a pulmonary tumour and 2 rats (4.7%) a mesothelioma.	Davis 1996 (Miller 1999a) Cullen 1997
Wistar rats (n=24 / sex)	JM100 (type 475)	5 mg/m^3	332 f/cm^3		5h/d 5d/wk whole-body	12 mo + 4, 7, 12 or 16 mo obs. 24 mo + 4 mo obs.	• Dimensions : 97% < 5µm in length and 43% < 0.1 µm in diameter • No tumours in JM100 and control groups • 9/47 rats (19%) with pulmonary carcinoma in the chrysotile group • No data on survival	Le Bouffant 1984
Rats	JM100 (type 475)	10 mg/m^3	9625 f/cm^3			24 mo	• Dimensions : 52%>10µm in length and 43%<0.1 µm in diameter • No tumours • No positive or negative control groups	Le Bouffant 1987

Female Wistar rats (n=108)	104/475 (type 475)	3.0 mg/m^3	252 f/cm^3		5h/d 4d/wk nose-only	12 mo	• Median dimensions: 4.8 µm in length and 0.42 µm in diameter. 90%<12.4µm in length • Lung burden: 0.4 mg after 6 months, 0.6 mg after 12 months and 0.2 mg after 12 additional recovery months. • Half-life about 600 days (vs 200 days for crocidolite). 60% (35% with length>5µm) of the fibres in the lung at the end of exposure were remaining after 12 additional months. • 1/107 pulmonary tumour (1/50 for crocidolite, 0/50 for chrysotile and 0/105 for control groups)	Muhle 1987
Fisher 344 rats (n=50 / sex)	JM100 (type 475)	10 mg/m^3			7h/d 5d/wk whole-body	12 mo + lifetime obs.	• No data on dimensions • No pulmonary tumours (n=55) in the JM100 group, 3/53 (6%) in the control group and 11/56 (20%) in the chrysotile group.	McConnell 1984
F344 rats (n=100)	100/475 (type 475)	5 mg/m^3	-	-	7h/d 5d/wk whole-body	86 w	• Dimensions: diameter < 3.5 µm; group 3: length > 10 µm and group 4: length < 10 µm • No fibrosis observed • Macrophages aggregates and granulomas resulting in plaque-like foci in pleural and subpleural locations • No mesothelioma or pulmonary tumours reported in the control and exposed groups • Elevated mononuclear cell leukaemia: 35/99 (35.4%, $p<0.05$) and 42/99 (42.4%, $p<0.01$) in groups 3 and 4, compared to 21/99 (21.2M) in the control group.	Moorman 1988
Female Osborne-Mendel rats (n=52-61)	JM100 (type 475)	2.4 mg/m^3	3000 f/cm^3		6h/d 5d/wk nose-only	24 mo	• Median dimensions : 4.7µm in length (mean=7.5) and 0.45µm in diameter (mean=0.4) • No tumours in JM100 and control groups • 3/57 tumours (5%) in the crocidolite group (1 mesothelioma and 2 carcinomas)	Smith 1987

Fisher 344 rats (n=48)	JM100 (type 475)	10 mg/m^3	1436 f/cm^3	approx. 108 f/cm^3	7h/d 5d/wk	12 mo expo. + 0 mo, 12 mo or lifetime obs.	• Dimensions : 29% > 10µm in length • Wagner grades of lung fibrosis at 12/16 months and 24 months after the start of exposure was respectively 3.0 and 3.3 for 475-glass and 4.1 and 4.0 for chrysotile. Rats which died spontaneously generally showed a slight increase in the degree of fibrosis seen. • 1/48 rats had a pulmonary adenocarcinoma (2%) in the period 500-1000 days after the start of exposure. 3 had bronchoalveolar hyperplasia. • Controls: no tumour (n=48) • Chrysotile: 11/48 rats (23%) had adenocarcinomas and 5 bronchoalveolar hyperplasia • Inadequate data on survival	Wagner 1984
Male Golden Syrian hamster (n=83)	MMVF33 (type 475)	37 mg/m^3	310 f/cm^3	109 f/cm^3	6h/d 5d/wk nose-only	78 wk + 6 wk recovery	• 1 day after a 6 h exposure, lung burden was $11.5x10^5$ WHO fibres and $2.2x\ 10^5$ 20 µm-length fibres. • No significant increase in lung weight at week 13 and 52 but 20-30% heavier than control at the end of the study. • Cell proliferation at bronchoalveolar duct junction was increased at weeks 13 (but not after an additional 13-week recovery), 52 and 78. • In the lung, mild excess of macrophages concentrated at bronchoalveolar junctions at week 13 (Wagner grade=2.6). Progression of inflammatory changes accompanied by mild interstitial fibrosis at weeks 26 (Wagner grade=3.5), 52 and 78 (Wagner grade=4.0) • Collagen deposition in the pleura of all animals at 6 and 12 months. This effect is no more statistically significant after 78 weeks exposure + 6 weeks recovery. • After recovery, inflammatory lesions regressed but pulmonary or pleural fibrosis did not. • After 78 weeks, a significant number of fibres were found in	McConnell 1999 (Hesterberg 1997)

							diaphragm (995 WHO fibres/mg) and thoracic wall (151 WHO fibres/mg). • 1 hamster (2%) died at 7.5 months and had a mesothelioma with 475-glass exposure. Mesothelial hyperplasia was found in 18 animals (21.7%). • No pulmonary or mesothelial neoplasm in the control group • Amosite induced mesotheliomas: 3/83 (4%) in the low-dose (0.8 mg/m^3), 22/85 (22% in the mid-dose (3.7 mg/m^3) and 17/87 (20%) in the high-dose (7.1 mg/m^3) groups	
Male Syrian golden hamster (60-70)	JM100 (type 475)	2.4 mg/m^3	3000 f/cm^3		6h/d 5d/wk nose-only	24 mo	• Median dimensions : 4.7 µm in length (mean=7.5) and 0.45 µm in diameter (mean=0.4) • No pulmonary tumours with 475-glass • 1/58 carcinoma in the control group and 0/58 in the crocidolite group.	Smith 1987
Baboons (n=10)	JM 102/104 (102 =type **475**, 753) (104= type **475**, 753, **E**)	1000 f/cm^3				30 mo	• No tumours in exposed and control animals • Peribronchiolar fibrosis in animals exposed to JM 102/104 and crocidolite	Gold-stein 1984
Cynomolgus monkeys (n=12)	100/475 (type 475)	5 mg/m^3	-	-	7h/d 5d/wk whole-body	18 mo (=72 weeks)	• Dimensions: diameter < 3.5 µm; group 3: length > 10 µm and group 4: length < 10 µm • No changes in pulmonary function parameters • Macrophages aggregates in lung and tracheobronchial lymph nodes • No mesothelioma or pulmonary tumours reported	Moor-man 1988

4.9.1.3 Carcinogenicity: intraperitoneal

Species	Fibre type	Dose			Injection schedule	Duration of observa-tion	Observations and Remarks	Ref.
		Total	WHO	L>20 µm				
Female Wistar rats (n=44)	JM104/E (E) JM 475 (type 475)	2 or 10 mg 2 mg	-	-	2 or 10 mg 2 mg	lifetime	• E-glass: 14/44 (32%) and 29/44 (66%) rats with abdominal tumours at doses of 2 and 10 mg, respectively • 475-glass: 2/44 (4%) rats with abdominal tumours (dimensions: median length=10 µm and median diameter=0.2 µm) • Chrysotile: 9/44 (20%), 26/44 (59%) and 35/44 (79%) rats with abdominal tumours at doses of 0.4, 2 and 10 mg, respectively	Pott 1984
Male Wistar rats (n=24)	100/475 (type 475)	8,3 mg	1868 $x10^6$ f	9 $x10^6$ f	1 x 8,3 mg (in 2 ml saline)	lifetime	• Mean diameter: 0.32 µm • 8/24 animals (33%) developed mesothelioma, compared to 21/24 (88%) with amosite. • No negative control	Davis 1996 (Miller 1999b)
Female Osborne -Mendel rats	JM 100 (type 475)	25 mg			1x25 mg in 0.5 mL saline	lifetime	• Dimensions: median length: 4.7 µm and median diameter: 0.4 µm • Mesotheliomas in 8/25 JM100-treated rats (32%), 20/25 crocidolite-treated rats (80%) and 0/150 control rats	Smith 1987
Female Sprague-Dawley rats	104/475 (type 475)	2 -10 mg			1 injection (in 2 ml saline)	lifetime	• Dimensions: median length=2.4 µm and median diameter=0.33 µm • Sarcomas, mesotheliomas and carcinomas were seen in 21/54 (39%) and 24/53 (45%) animals treated with 2 and 10 mg, respectively • Control: 3/54 animals (5.5%) had tumours	Pott 1987

Female Wistar rats	104/475 (type 475)	0.5 – 2 mg			1 x 0.5 or 2 mg	lifetime	• Dimensions: median length=3.2 µm and median diameter=0.18 µm • 5/30 (17%) and 8/31 (26%) animals treated with 0.5 or 2 mg had abdominal tumours • Crocidolite: 18/32 (56%) and 28/32 (87%) rats with abdominal tumours at doses of 0.5 and 2 mg, respectively • Saline-control group: 2/32 rats (6%) had tumours	Pott 1987
Female Wistar rats	JM 475 (type 475)	5 mg	680 x10^6 f			130 weeks	• Dimensions: median length=2.6 µm and median diameter=0.15 µm • 34/53 treated rats (64%) had tumours (excluding uterine tumours) and 2/102 control rats (2%) had mesotheliomas	Pott 1989
Female Wistar rats (n=46-48)	JM 475 (type 475)	-	0.33 x10^9 f	-			• 17 of treated rats (36%) developed abdominal tumours • Control (saline): 2/50 had tumours	Pott 1991
Female Wistar rats	JM104 (types 475, 753, E)				2, 10 or 2x25 mg	lifetime	• Dimensions: median length=10 µm and median diameter=0.2 µm • 2 mg-dose: 17 rats had mesothelioma, 3 a sarcoma (n=37). Total tumour rate: 27.4% • 10 mg-dose: 36 rats had mesothelioma, 4 a sarcoma and 1 a carcinoma (n=77). Total tumour rate: 53.2% • 2x25 mg-dose: 47 rats had mesothelioma, 8 a sarcoma (n=77). Total tumour rate: 71.4% • crocidolite group (2 mg): 15/39 abdominal tumours (38%)	Pott 1976
Rats	JM106 (types 475, 753, E)				2, 10 or 4x25 mg	lifetime	• Dimensions: median length=3 µm and median diameter=0.4 µm • 2 mg-dose: 1 rat had a mesothelioma (n=34). Total tumour rate: 2.9% • 10 mg-dose: 2 rats had mesothelioma, 2 a sarcoma (n=36). Total tumour rate: 11.0% • 4x25 mg-dose: 20 rats had mesothelioma, 3 a sarcoma (n=32). Total tumour rate: 72%	Pott 1976

4.9.1.4 Carcinogenicity: intratracheal

Species	Fibre type	Dose			Injection schedule	Duration of observation	Observations and Remarks	Ref.
		Total	WHO	L>20 µm				
Female Wistar rats	104/475 (type 475)	10 mg			20 x 0.5 mg in 0.3 mL saline	Lifetime	• Dimensions: median length=3.2 µm and median diameter=0.18 µm • Lung tumours in 5/34 (15%) treated animals (1 adenoma and 4 carcinomas) • 0/40 in control animals • 15/35 in the crocidolite group (43%)	Pott 1987
Female Osborne-Mendel rats (n=22)	JM100 (type 475)	10 mg			5 x of 2 mg in 0.2 mL saline (weekly)	Lifetime	• Dimensions: mean length=4.7 µm and mean diameter=0.4 µm; 19% > 10µm in length • No tumour in controls and JM100-treated animals • 2/25 in crocidolite-treated animals (8%)	Smith 1987
Syrian golden hamster (n=35 / sex)	JM 104 (types 475, 753, E)	26 mg			26 x 1mg in 0.2 mL 0.005% gelatine in saline (every 2 wk for 52 wk)	85 wk	• Dimensions: 58% < 5 µm in length, 88%< 1.0 µm in diameter • No mesothelioma or pulmonary tumour in JM104- or crocidolite-treated groups	Feron 1985
Male Syrian golden hamster	JM 104 (types 475, 753, E)	8 mg			8 x 1mg in 0.15 mL saline (weekly)	113 wk	• Group with median length= 7 µm: 48/136 animals (35%) developed a tumour (5 lung carcinomas, 37 mesotheliomas, 6 sarcomas) • Group with median length= 4.2 µm: 38/138 animals (27%) developed a tumour (6 lung carcinomas, 26 mesotheliomas, 6 sarcomas) • Crocidolite: 18/42 rats (13%) had a tumour (9 lung carcinomas, 8 mesotheliomas, 1 sarcomas) • Control (TiO_2): 2/135 rats (1.5%) had sarcoma	Mohr 1984

4.9.1.5 Carcinogenicity: intrapleural

Species	Fibre type	Dose			Injection schedule	Duration of observation	Observations and Remarks	Ref.
		Total	WHO	L>20 µm				
Sprague Dawley rats (n=32-45)	JM 104 (types 475, 753, E)	20 mg			1 x 20 mg in 2 mL saline	Lifetime	• Dimensions: mean length=5.89 µm and mean diameter=0.229 µm • 6/45 animals (13%) had mesothelioma. • Chrysotile : 14/33 (42%), and crocidolite: 21/39 (54%) mesotheliomas • No thoracic tumours in 32 control animals.	Mon-chaux 1981
Sprague Dawley rats (n=48)	JM100 (type 475)	20 mg	30.2 x10^8 f		1 x 20 mg in 0.5 mL saline	Lifetime	• Dimensions: 88% < 5 µm in length and 98.5% ≤ 1 µm in diameter • 4/48 treated animals (8%) and 0/24 control animals had **mesothelioma** • Chrysotile: 6/48 mesotheliomas (12%)	Wagner 1984
Female Fisher rats (n=25)	JM100 (type 475)	20 mg			1 x 20 mg	2 to 430 days	• Dimensions: mean length=2.2 µm and mean diameter=0.15 µm • Chronic inflammation occurred in 9 rats (37.5%), fibrosis in 18 rats (75%), foreign body reaction in 10 rats (41.6%), mesothelial dysplasia in 9 (37.5%) and hyperplasia in 16 rats (66.6%). • 3 animals (12.5%) killed at day 102, 408 and 416 days after inoculation had mesothelioma	Fraire 1994
Wistar rats (n=16 / sex)	JM100 (type 475)	20 mg			1 x 20 mg in 0.4 mL saline	Lifetime	• Dimensions: mean length=1.7 µm and mean diameter=0.12 µm. 99% < 0.5 µm in diameter and 2%> 20 µm in length • 4/32 treated animals (12.5%) had mesothelioma, 0/32 in the control group.	Wagner 1976

4.9.1.6 Carcinogenicity: dermal

No data.

4.9.2 Human information

Study type	Fibre type	End point	Population	Exposure assessment	Observations and Remarks	Ref.
Case-control	Microfibres	Larynx and hypopharynx cancers	Patients recruited from 15 hospitals in 6 French cities. Larynx cancers: n=296 subjects Hypopharynx cancers: n=201 subjects Controls: n=295 with non-respiratory cancers	Job history was collected by face to face interview. Exposure was assessed using a job-exposure matrix and 2 categories were defined: Ever exposed or Never exposed	• Results adjusted for age, smoking and alcohol consumption • Laryngeal cancers: 16 cases/9 controls ever exposed; OR=1.28 (95% CI: 0.51-3.22) • Hypopharynx cancers: 7 cases/9 controls ever exposed; OR=0.78 (95% CI: 0.26-2.38) • No significant association between laryngeal or hypopharyngeal cancers and exposure to microfibres but exposure concerned only a few subjects.	Marchand 2000
Historical cohort	Fibre glass including 2/10 plants producing special-application glass fibres	Respiratory system cancers	32,110 production or maintenance workers employed for 1 year or more between 1945 and 1992. Control: US or local county mortality rates	Quantitative estimation of fibre exposure.	• No evidence of excess mortality risks for all causes of death, all cancer death or non malignant respiratory disease mortality. • General cohort: a 6% (SMR=1.06, 95% CI: 1.00-1.14, p=0.05) and 16% (SMR=1.16, 95% CI: 1.08-1.24, p<0.01) excess of respiratory system cancer mortality was observed compared to respectively local and national rates. • Duration of exposure and cumulative exposure were not associated with an increased risk of respiratory system cancer. • Possible co-exposure to arsenic, asbestos, asphalt, epoxy, formaldehyde, PAH, phenolics, silica, styrene and urea. • Special-purpose glass fibres exposure category: SMR=1.09, 95% CI: 0.87-1.36 (n=81 cases)	Marsh 2001 (IARC 2002)

4.9.3 Other relevant information

Test	Fibre type	Cell system	Protocol	Conc. (mg/l)	Observations and Remarks	Ref.
Cyto-toxicity	JM100 (type 475)	Rat alveolar macrophages	24, 48 or 72h.	0-100-200-300 µg/ml	• Cell viability (trypan blue exclusion): dose-related decrease of cell viability at all doses and time points. • Membrane integrity: significant dose-dependent increase of LDH and β-gal release • Macrophage function: significant dose-dependent decrease of Zymosan-stimulated oxygen and hydrogen peroxide consumption.	Castra-nova 1996
Cyto-toxicity	JM100 (type 475)	Rat alveolar macrophages	18 h	0-50-100-250-500 µg/ml	• Macrophage function: chemiluminescence (measure of superoxide release) was significantly decreased at 250 and 500 µg/ml. • Macrophage cytotoxicity: LDH release was significantly increased at 250 and 500 µg/ml. • Longer fibres (mean length of 17 and 33 µm) appear to be more toxic	Blake 1998
Cell activation	JM100 (type 475)	A549 cells	20 h	0-5-10-15-25-50 µg/ml	• Marked dose-dependent cytotoxicity • No change in the expression of p53, Cip1 and Gadd153 proteins (proteins associated with DNA damage). Increase with IUCC crocidolite.	Johnson 1997
Cell activation	100/475 (type 475) 104E (E)	Rat alveolar macrophages	24 h	8.2×10^6 fibres (WHO)	• Both microfibres showed an intermediate activity with a TNF-α production of 60 (475-glass) and 71 (E-glass) TNF-α unit/10^6 cells. Two silicon carbide whiskers and two asbestos samples were more active while RCF and other MMVF tested were inactive.	Cullen 1997
Cell activation	Code 100 (475)	Rat alveolar macrophages Hamster tracheal epithelial cells	1 h 3 h	2.5 to 25 µg/cm^2 0.1 to 20 µg/cm^2	• Inflammatory capability: significant dose-related increases of superoxide anions release from 5 µg/cm^2 • Membrane integrity: significant dose-related increases of ^{15}Cr release from 1 µg/cm^2	Moss-man 1990
Cell activation	100/475 (type 475)	Hamster and rat alveolar macrophages		2.5 µg/ml or 5 µg/cm^2	• Induction of superoxide anions release	Hansen 1987
Cell activation	JM100 (type 475)	Rat alveolar macrophages		3×10^7 f/ml	• Inhibition of the superoxide anions release by both naked or IgG-coated fibres	Brown 1998

Cell activation	JM100 (type 475)	Mouse monocyte macrophage cell line RAW 264.7		3.0×10^8 2.0×10^7 f/ml	• Production of TNF-α factor and activation of transcription factor • Effects were more important with longer fibres (17 µm) than with shorter fibres (7µm)	Ye 1999
Cell activation	100/475 (type 475)	Rat alveolar macrophages, human blood monocytes, THP-1 human macrophages cell line, mouse macrophage cell line		3×10^7 f/ml	• No significant increase of TNF-α release	Fisher 2000

4.9.4 Summary and discussion of carcinogenicity

Glass fibres of the type of which '475' is considered representative induced by **inhalation** in rats few benign pulmonary tumours only (Davis 1996). This result confirms previous experiments in which no significant increase of the tumour incidence with exposure to fibres of type '475' was observed. However, several important limits were identified in these studies including insufficient exposure duration (Le Bouffant 1984, Muhle 1987, Moorman 1988, Wagner 1984), use of short fibres samples (Le Bouffant 1984, Muhle 1987, Smith 1987), no data on fibre dimensions (McConnell 1984), no positive asbestos control group (Le Bouffant 1987, Moorman 1988), no data on animal survival (Le Bouffant 1984, Wagner 1984). The absence of a significant induction of tumours with asbestos (crocidolite or chrysotile) in Muhle (1987, wistar rats) and Smith (1987, Female Osborne-Mendel rats and Male Syrian golden hamsters) long-term inhalation studies strongly questions the relevance of these studies in the present evaluation.

In hamster studies, Smith (1987) observed no tumour in animals exposed to both glass fibres of type '475' or crocidolite. However, in the recent study by McConnell (1999) with a 18-month exposure, 1 hamster (2%) had a mesothelioma. It was accompanied by pleural fibrosis and mesothelial hyperplasia in 22% of the animals.

Two **inhalation** studies were performed by Goldstein (1984) and Moorman (1988) using monkeys (baboons and Cynomolgus monkeys respectively). No tumours were reported after respectively 18 months (Moorman 1988) and 30 months (Goldstein 1984) of exposure and animals were sacrificed at the end of the exposure. Longer exposures and observations would have been required to detect neoplasms in such species.

Several studies are available on rats by the **intraperitoneal (IP) route for type '475' glass fibres**. In all studies, an increased incidence of abdominal tumours, mesotheliomas, sarcomas and lung carcinomas was observed (Pott 1976, 1984, 1987, 1989, 1991, Davis 1996, Miller 1999b, Smith 1987). When two levels of dose are used, a positive trend between tumour incidence and exposure is observed (Pott 1976, Pott 1984, Pott 1987). It should however be noted that the type of glass (475, E or 753) is not indicated in Pott 1976.

One study on glass fibre of type '475' did not report increased incidences of lung tumours following **intratracheal instillation** fibres in rats (Smith 1987) but in these studies, the crocidolite control-groups were also negative. Two other studies reported lung tumours in 15% of exposed rats (Pott 1987) and 27% or 35% of exposed hamsters (Mohr 1984) with an increased incidence with longer fibres. It should also be noted that the type of glass (475, E or 753) is not indicated in the hamster studies.

Following massive **intrapleural injection** of **glass fibres of type '475'**, mesotheliomas were consistently reported in 8 to 12% of the animals in three different rat studies (Wagner 1984, Fraire 1994, Wagner 1976). In Fraire 1994, fibrosis was also observed in 75% of animals and mesothelial hyperplasia in 66%.

The reach registration dossier reported the rat chronic/carcinogenicity studies of McConnell (1994), Wagner (1984) and Le Bouffant (1987). All three studies are concluded to be negative in terms of carcinogenic potential.

Classification by IARC in 2002:

In its evaluation, IARC (2002) concluded that there is sufficient evidence in experimental animals for special-purpose glass fibres including E-glass and glass fibres of type '475' and classified them as possibly carcinogenic to humans (group 2B), as for refractory ceramic fibres.

Human data:

A case-control study did not show any association between laryngeal or hypopharyngeal cancers and microfibre exposure (Marchand 2000) but the study included a very small number of microfibre-exposed subjects. In an historical cohort study (Marsh 2001), an excess of respiratory cancer was observed in the general fibre glass group but not in the special–purpose glass fibres sub-group. The size of this sub-group was also limited. Overall, these data are not considered sufficient to draw any conclusion on the potential carcinogenic effects in humans.

4.9.5 Comparison with CLP criteria

The **epidemiological data** do not bring sufficient evidence of carcinogenicity in human.

For experimental data, the CLP criteria for classification establish different levels of evidence:
— "***sufficient evidence of carcinogenicity****: a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide sufficient evidence. A single study in one species and sex might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites;*
— ***limited evidence of carcinogenicity****: the data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is*

restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs."

IARC (2002) reported that 'many intraperitoneal studies of special-purpose glass fibres have been conducted, most of which have examined the tumorigenic potential of two compositions of special purpose glass fibres ('475' and E-glass fibres) after injection or surgical implantation of fibres at high doses (approximately 109 fibres) into the peritoneal cavity of rats. All of these studies reported an increase in peritoneal tumours'. The present analysis shows a carcinogenic potential by the intraperitoneal (E and type '475'), intratracheal (data on type '475' only) and intrapleural (data on type '475' only) routes of exposure. Fibre biopersistency may enable their migration following inhalation into the pleural cavity and emphasise the relevance of positive results by the intrapleural route.

Although carcinogenicity potential is confirmed by inhalation in a well-designed study with E-glass fibre, no study clearly demonstrates the induction of tumour following inhalation of type '475' glass fibres and most of the available studies show important limitations.

On the basis of animal studies by inhalation, E-glass fibres induce marked macrophage reaction, alveolar fibrosis and hyperplasia which may indicate a progressive pathway to neoplastic transformation of respiratory cells whereas type '475' glass fibres do not exhibit such effects by inhalation (Cullen, 2000). Besides, comparison between the carcinogenic potential of both fibres by intraperitoneal route (Pott 1984) shows that 32% of rats has abdominal tumours with E-glass although only 4% of rats has abdominal tumours with type 475-glass tumours.

4.9.6 Conclusions on classification and labelling

Overall, it is concluded that glass fibres of representative composition and physical characteristics (which includes '475' type and other special purpose glass fibres like 'Evanite B' and 'Laucher B-glass') but not E-glass fibres are suspected to be human carcinogens and should be classified as Carc. 2 (H351) under the CLP Regulation.

RAC evaluation of carcinogenicity

Summary of the Dossier submitter's proposal

Glass microfibres of representative composition [Calcium-aluminium-silicate fibres with random orientation with the following composition (% given by weight): SiO2 55.0-60.0%, Al2O3 4.0-7.0%, B2O3 8.0-11.0%, ZrO2 0.0-4.0%, Na2O 9.5-13.5%, K2O 0.0-4.0%, CaO 1.0-5.0%, MgO 0.0-2.0%, Fe2O3 <0.2%, ZnO 2.0-5.0%, BaO 3.0-6.0%, F2 <1.0%] were proposed by the DS to be classified as Carc. 2; H351. The DS further proposed adding note R, which, according to Annex VI of the CLP Regulation, states that the classification as a carcinogen needs not apply to fibres with a length weighted geometric mean diameter less two standard geometric errors greater than 6 µm.

The DS presented the available studies by different routes of exposure (inhalation, intraperitoneal, intratracheal, intrapleural) as well as a summary of the available human information. The DS concluded that no study clearly demonstrated the induction of tumours following inhalation of glass microfibres of representative composition (microfibres analogous to commercial grade or type '475'). However most of the available

studies have considerable limitations.

Overall, the DS concluded that glass microfibres of representative composition are suspected to be human carcinogens and should be classified as Carc. 2 (H351) under the CLP Regulation with note R assigned to the new entry in Annex VI of CLP.

Comments received during public consultation

No comments were submitted objecting to the proposed classification. Two MSCAs supported classification but suggested some editorial improvements. One industrial organisation indicated a need to rename the substances from "fibres" to "microfibres" which was supported by the DS and also taken into account in this opinion. One industrial organisation pointed out two references already included in the CLH report which provided data supporting different classifications for E-glass microfibres and glass microfibres. The CLH report will however not be updated but additional information is available in Annex 2 to the opinion (Response to comments document, RCOM).

Assessment and comparison with the classification criteria

Summary of animal studies

Inhalation studies:

In none of the several inhalation toxicity studies on rats exposed for 12-30 months to glass microfibres (microfibres analogous to commercial grade or type '475') was any significant increase in lung tumour or lung fibrosis frequency observed (Davis, 1996; Miller, 1999a; Cullen, 1997; Le Bouffant *et al.*, 1984; Le Bouffant *et al*., 1987; Hesterberg, 1997; Muhle, 1987; McConnel, 1984, 1999; Moorman, 1988; Smith, 1987; Wagner, 1984).

However, as the DS pointed out, several important limitations were identified in these studies such as insufficient exposure duration (Muhle *et al*., 1987, Moorman *et al*., 1988), use of short fibres as test materials (Le Bouffant, 1984, Muhle *et al*., 1987, Smith *et al*., 1987), no data on fibre dimensions (McConnell *et al*., 1984), no (asbestos) positive control group (Le Bouffant *et al.* 1987, Moorman *et al*., 1988) and no data on animal survival (Le Bouffant, 1984 Wagner *et al*., 1984). The absence of a significant induction of tumours with asbestos in Muhle *et al*. (1987) and Smith *et al*. (1987) raises questions concerning the relevance of these studies in the present evaluation.

The detailed review (Bernstein, 2007) of the available toxicology data on glass microfibres (such as type '475' special-purpose glass fibres) clearly showed that following inhalation of these fibres even at relatively high doses, the glass microfibres '475' were not fibrogenic and did not cause tumours. The available data clearly showed pathological differences between the glass microfibres analogous to grade or type '475' and the E-glass microfibres and support treating these two types of fibres independently.

The greater pathology induced by the E-glass microfibres, referred to as commercial type grade or type '104E', compared to glass microfibres (commercial grade or type '100/475' microfibres), might be partly explained by the greater numbers of long fibres retained in the lung after 12 months of inhalation. However, it is possible that modification of surface properties by extensive selective leaching of some glass components reduces the toxic potential of the commercial grade or type '100/475' microfibres.

At the end of 12 months of exposure, the mean number of grade or type '104E' fibres of all lengths in the lungs was approximately double that for amosite, but two-thirds of that for '100/475' microfibres. For fibres longer than 15 µm, the mean grade or type '104E'

burden was similar to that for the amosite and more than twice that of the '100/475' fibres. After a 12-month recovery period, the retained lung burdens (of fibres of all lengths) were approximately 30% of those at 12 month for both microfibres, and somewhat higher (approximately 44%) for amosite. Amosite and '100/ 475' fibres longer than 15 µm were more persistent in the lungs than grade or type '104E' fibres.

The chemical composition of grade or type '104E' fibres did not appear to have been significantly altered by up to 24 months of residence in lung tissue, whereas the composition of type '475' was substantially altered over the same time period.

In a parallel intraperitoneal injection study, grade or type '104E' caused considerably more mesotheliomas (21 rats out of 24) than 100/475 (8 rats out of 24). In addition, grade or type '104E' appeared to be more active than amosite asbestos, since mesotheliomas appeared much more quickly in the grade or type '104E'-treated animals. The results of this study demonstrated that two microfiber types, '100/475' and '104 E', of similar dissolution rates, had markedly different potency in rats. In the opinion of the authors (Cullen *et al*., 2000), this contrast is only partly due to differences in numbers of long fibres and that differences in surface properties of the fibres, possibly due to proportionately greater leaching of '100/475' fibres, play an important role.

In hamster studies, Smith *et al*. (1987) observed no tumours in animals exposed to microfibres analogous to type '475' glass (2.4 mg/m^3, 3000 f/cm^3, median dimensions: 4.7 µm in length (mean 7.5 µm) and 0.45 µm in diameter (mean 0.4 µm), 6h/d, 5d/week) or crocidolite for 24 months.

In the study by McConnell *et al*. (1999) with exposure to 37 mg/m^3 microfibres analogous to type '475' for 78 weeks (310 f/cm^3; 109 f/cm^3 with L > 20 µm, 6h/d, 5d/week), 1 hamster (2%) had a mesothelioma. It was accompanied by pleural fibrosis and mesothelial hyperplasia in 22% of the animals.

Two inhalation studies were performed on monkeys exposed to microfibres analogous to type '100/475'. The monkeys were sacrificed at the end of the exposure (Moorman *et al*., 1988; Goldstein *et al*., 1984). No tumours were reported in cynomolgus monkeys after 18 months of exposure to 5 mg/m^3 (dimensions: diameter < 3.5 µm; group 3: length > 10 µm and group 4: length < 10 µm, 7h/d, 5d/week) (Moorman *et al*., 1988) or in baboons after 30 months of exposure to 1000 f/cm^3 (Goldstein *et al*., 1984). Longer exposures and observation periods would have been required to detect neoplasms in such animals. Peribronchiolar fibrosis was observed in the study from Goldstein *et al*. (1984).

Overall it is concluded that there is not sufficient evidence of carcinogenicity of glass microfibres of representative composition (microfibres analogous to type '475') in inhalation studies on animals.

Intratracheal studies:

Two intratracheal instillation studies in hamsters were reported by the DS in the CLH report, but the exact type and composition of glass microfibres used (types '475', 'E' or '753') was not indicated by the authors (Feron *et al*., 1985; Mohr *et al*., 1984). They are inconclusive for the hazard assessment of E-glass microfibres.

One study on microfibres analogous to type '475' glass fibres did not report increased incidences of lung tumours 5 weeks following intratracheal instillation of a total of 10 mg '475' glass fibres (instillations of 2mg/day for 5 days/week) in rats observed over their lifetime (Smith *et al*., 1987), but in this study only 8% of animals (2/25) in the crocidolite positive control-group had tumours.

In the other study, in 15% of the rats receiving intratracheally in total 10 mg glass

microfibres (microfibres analogous to type '475', 20 x 0.5 mg) reported lung tumours (1 adenoma, 4 carcinomas), while no tumours were observed in 40 negative control animals and a 43% tumour incidence was reported in the crocidolite positive control group (Pott *et al*., 1987).

Two intratracheal instillation studies in hamsters were reported by the DS in the CLH report, but the exact type and composition of glass microfibres used (types '475', 'E' or '753') was not indicated by the authors (Feron *et al*., 1985; Mohr *et al*., 1984) suggesting that these fibres were administered together. An overview of the study results after intratracheal instillation is provided in the Table below.

Tumour incidences (%) in animals after intratracheal instillation of glass microfibres in rats and hamsters (in bold; where applicable, negative control was TiO2; positive control was crocidolite asbestos)

Reference and species	Type of microfibres used in the study	Number and percentage of Tumours (lung tumours and mesotheliomas)
Pott, 1987 (rat)	'475' crocidolite	**5/34 (15%)** (1 adenoma, 4 carcinomas) 15/35 (43%)
Smith, 1987 (rat)	'475' crocidolite	**0%** 8%
Feron, 1985 (hamster)	'475', '753' and/or E glass fibres (mixture or chemical composition unknown)	**0** **(0%)**
Mohr, 1984 (hamster)	'475', '753' and/or E glass fibres (two lengths, mixture or chemical composition unknown) crocidolite TiO_2	**48/136 (35%)** (with median fibres length of 7µm) **38/138 (27%)** (with median fibres length of 4.2 µm) 18/42 (13%) 2/135 (1.5%)

In the absence of identification of the specific type of glass fibres and information on their composition in some of the studies, it is concluded that results of these studies using intratracheal instillation do not provide sufficient evidence of their carcinogenic potential by this route of exposure.

Intraperitoneal injection studies:

Several studies are available on rats (mainly Wistar) by the intraperitoneal (IP) route for '475' glass microfibres and E-glass microfibres. In all studies, the animals received a single IP injection ranging from 2 to 25 mg '475' glass fibres or mixture of '475', 'E' and '753' glass fibres. The animals were kept for lifetime observation (limited to 130 weeks in the study from Pott, 1989). It should also be noted that the the mixture of '475', 'E' and '753' was applied in studies of Pott et al. (1976) and Pott (1984).
In Pott et al. (1976), the median fibre length was either 10 µm or 3 µm and the median diameter was 0.2 µm or 0.4 µm, respectively, in the two parts of the study.
In Pott et al. (1984) the dimensions of '475' glass fibres were: median length = 10 µm and median diameter = 0.2 µm.
In Pott (1987, high dose) the median length of the '475' glass fibres were 2.4 µm and the median diameter was 0.33 µm.
In Pott et al. (1987, low dose) the median length of the '475' glass fibres were 3.2 µm and the median diameter was 0.18 µm.
In Pott et al. (1989) the median length of the '475' glass fibres was 2.6 µm and the median diameter was 0.15 µm.
In Davis et al. (1996) the mean diameter of the '475' glass fibres were 0.32 µm.

In Smith et al. (1987) the dimensions of the '475' glass fibres were: median length: 4.7 µm and median diameter 0.4 µm.

In the study of Pott (1984), E-glass microfibres at doses of 2 and 20 mg caused abdominal tumours in 32% of rats (14/44) and in 66% of rats (29/44), respectively. Chrysotile induced abdominal tumours in 20% of rats (9/44), 59% of rats (26/44) and in 79% of rats (35/44) at doses of 0.4, 2 and 10 mg, respectively. Type '475' glass microfibres induced abdominal tumours in 4 % of rats (2/44).

An increased incidence of abdominal mesotheliomas (4%) and sarcomas (64%) was observed in rats dosed intraperitoneally with 2 mg, 10 mg or 4x25 mg of '475' glass microfibres (Pott *et al*., 1984, 1987, 1989, 1991, Davis *et al*., 1996, Miller *et al*., 1999b, Smith *et al*., 1987). The frequency of abdominal tumours in saline-treated control rats were in the range of 0-6%. When two dose levels were used, a positive trend between tumour incidence and dose was observed (Pott *et al*., 1976, 1984 and 1987).

It is concluded by RAC that the results of the studies demonstrate carcinogenicity of glass microfibres after intraperitoneal application, although carcinogenic potential of glass microfibres of representative composition analogous to type '475' by this route is significantly less than that of E-glass microfibres and asbestos (chrysotile, crocidolite).

Intrapleural injection studies

Four groups of 25 BALB/c mice (sex and age unspecified) received single intrapleural injections of a high dose of 10 mg of one of four different samples of borosilicate glass fibres (chemical composition not given) in 0.5 mL distilled water. The material for injection was obtained by separating each of two original samples with average diameters of 0.05 µm and 3.5 µm into two samples, one with lengths of several hundred microns and the other with lengths of < 20 µm. Animals were killed at intervals of two weeks until 18 months of exposure (a total of 37 mice survived at this time). No pleural tumour was found in any of the treated animals, whereas mesotheliomas were observed in 2/150 mice given intrapleural injections of chrysotile or crocidolite (dose not stated) in a parallel experiment. The IARC Working Group noted the small number of animals used, the relatively short observation time and the low response in the positive controls (Davis, 1976 quoted from IARC (2002)).

Groups of 32–36 SPF Wistar rats (twice as many males as females), 13 weeks of age, received single intrapleural injections in 0.4 mL saline of 20 mg glass fibre (a borosilicate; 30% of fibres 1.5–2.5 µm in diameter; maximum diameter, 7 µm; 60% > 20 µm in length) (chemical composition not given), 20 mg glass powder (a borosilicate; diameter < 8 µm) or 20 mg of one of two different samples of Canadian SFA chrysotile. Rats were kept until natural death; the average survival times were 774, 751, 568 and 639 days for the groups treated with glass fibres, glass powder and the two chrysotile samples, respectively. No injection-site tumour was observed in the group treated with glass fibres; a single mesothelioma occurred in the group treated with glass powder (after 516 days). The incidences of tumours in the two groups treated with chrysotile were 23/36 and 21/32; the first deaths of animals with tumours occurred after 325 and 382 days (Wagner *et al*., 1973 quoted from IARC, 2002).

Three groups of 16 male and 16 female Wistar rats, 10 weeks of age, received single intrapleural injections of 20 mg of fine US 'JM 100' glass fibres (type '475', 99% of fibres < 0.5 µm in diameter; median diameter, 0.12 µm; 2% > 20 µm in length; median length, 1.7 µm) (chemical composition not given) or a coarser "US" 'JM 110' glass fibres (type '475', 17% of fibres < 1 µm in diameter; median diameter, 1.8 µm; 10% > 50 µm in length; median length, 22 µm) (chemical composition not given) in 0.4 mL saline or saline alone.

Animals were kept until natural death; mean survival times were 716, 718 and 697 days for the mice treated with fine fibres, coarse fibres and saline, respectively. Between 663 and 744 days after inoculation, 4/32 animals given the finer glass fibres had mesotheliomas. No pleural tumours occurred in animals treated with the coarser glass fibres or in controls that received saline (Wagner *et al*., 1976 quoted from IARC, 2002).

According to the CLH report, there is a study on 'JM 104' type fibres (Monchaux *et al*., 1981 reported by IARC, 2002) conducted by the intrapleural route with uncertain significance for the assessment of the carcinogenicity of glass microfibres. In that study, groups of 32–45 male SPF Sprague-Dawley rats, three months of age, received single intrapleural injections of 20 mg of 'JM 104' type of glass fibres (consisting of types 475, 753, E) (chemical composition not given) (mean length, 5.89 µm; mean diameter, 0.229 µm), 20 mg UICC chrysotile A (mean dimensions, 3.21 µm x 063 µm), 20 mg UICC crocidolite (mean dimensions, 3.14 µm x 0.148 µm) in 2 ml saline or 2 ml saline alone. Animals were kept until natural death; the mean survival times for whole groups (and for animals with tumours) were 513 (499), 388 (383), 452 (470) and 469 days, respectively. The incidences of thoracic tumours were as follows: the group that received glass fibres, 6/45 (mesotheliomas); groups treated with chrysotile and crocidolite, 15/33 (1 carcinoma and 14 mesotheliomas) and 21/39 (mesotheliomas), respectively. No thoracic tumours occurred in the 32 control animals (Monchaux *et al*., 1981 quoted from IARC, 2002).

Following intrapleural injection of glass fibres of type '475' (20 mg, single dose), mesotheliomas were consistently reported in 8 to 12% of the animals in three different rat studies (Wagner *et al*., 1984, Fraire *et al*., 1994, Wagner *et al*., 1976). In Fraire *et al*. (1994), fibrosis was also observed in 75% of animals and mesothelial hyperplasia in 66%.

An overview of the study results after intrapleural injection is provided in the Table below (from IARC, 2002).

Tumour incidences (%) and other respiratory lesions in rats after intrapleural injection of glass fibres of type '475'

Reference	Type of microfibres used in the study	Fibres length & diamater	Mesothelioma (neg. controls/pos. controls)	Chronic inflammation (and fibrosis)	Mesothelial dysplasia	Hyperplasia
Monchaux *et al*., (1981)	'475', 753 and/or E	Mean fibre length=5.89 µm and mean diameter =0.229 µm	13 (0/42-54)	-	-	-
Wagner (1984)	'475'	88% <5 µm in length and 98.5 < 1 µm in diameter	8 (0/12)	-	-	-
Fraire (1994)	'475'	Mean length=2.2 µm and mean diameter =0.15 µm	12.5	37.5 (75)	37.5	66.6
Wagner (1976)	'475'	mean fibre length=1.	12.5 (4/32) vs. 0 in neg. controls (0/32)	-	-	-

		7 µm and mean diameter =0.12 µm				

It is concluded by RAC that the results of the studies demonstrate the carcinogenicity of glass microfibres after intrapleural application, although carcinogenic potency of glass microfibers of representative composition by this route is much less than that of E-glass microfibres and asbestos (chrysotile, crocidolite).

Summary of human studies

In a case-control study conducted by Marchand *et al*. (2000), 315 incident cases of laryngeal cancer, 206 cases of hypopharyngeal cancer, and 305 hospital-based controls with other types of cancer were recruited in 15 hospitals in six French cities. The subjects' past occupational exposure to asbestos and to four types of MMVF (mineral wool, refractory ceramic fibres, glass filaments, and microfibres) was evaluated based on their job history, with the aid of a job-exposure matrix. The authors concluded that asbestos and mineral wools (may) have a carcinogenic effect on the epilarynx and the hypopharynx. Due too few subjects exposed to these microfibers, the authors were unable to draw conclusions on their carcinogenicity.

In a historical cohort study (Marsh *et al*., 2001), a 6 % excess of respiratory system cancer compared to local rates (16 % compared to national rates) was observed in the general glass fibre group but not in the special–purpose glass fibres sub-group. The size of this sub-group was also limited (n=81).

Overall, as proposed by the DS, RAC concludes that these data are not considered sufficient to draw any conclusion on the potential carcinogenic effects in humans.

Comparison with the classification criteria

RAC recognised that glass microfibres which have the relevant dimensions and which are bio-persistent should be considered *de facto* carcinogenic. They are poorly soluble minerals which only undergo selective leaching and dissolution. Major determinants of toxicity are the form and size of the fibres, surface chemistry, and bio-persistence. Crystal structure, chemical composition, origin, and associated minerals, as well as trace contaminants, all modulate surface chemistry; and transformation, translocation, and solubility of the fibres in body fluids influence their bio-persistence, a factor which modulates cumulative exposure (IARC, 2012). In relation to fibre dimension and deposition, one can assume that there exists a continuum variation on the carcinogenic potency of respirable fibres, which increases with length. Bio-persistence of a fibre increases tissue burden, and therefore, may increase any toxicity the fiber might possess. For synthetic vitreous fibres, there is evidence from studies in animals that the potential for carcinogenicity increases with bio-persistence (IARC, 2012; WHO, 2005).

RAC also recognises that the relevant route of exposure for classification is inhalation which is also the major route of exposure in humans. Oral and dermal exposure routes are not considered relevant for glass microfibres. However, other non-physiological routes (e.g. intraperitoneal) and exposure regimens (e.g. single intratracheal administration) are considered relevant for hazard assessment. These non-physiological routes usually increase the sensitivity to a toxic response, mimicking worst-case exposure and bio-persistence. According to WHO (2005), carcinogenicity testing of fibres by intraperitoneal injection represents a sensitive assay compared with rat inhalation studies.

According to criteria of Annex 1 of the CLP Regulation (Table 3.6.1), in order to classify a substance in Category 2 for carcinogenicity i.e. suspected to have carcinogenic potential

for humans, classification should be largely based on animal evidence derived from animal experiments for which there is evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or 1B, based on strength of evidence together with additional considerations (see section 3.6.2.2 of CLP). Such evidence may be derived either from limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Taking into account the lack of carcinogenicity of glass microfibres of representative composition in several inhalation studies in rats, hamsters and monkeys, a very weak carcinogenic potential in intratracheal studies, some carcinogenic potential by intraperitoneal and intrapleural injections, RAC is of the opinion that glass microfibres of indicated representative composition warrant classification as Carc. 2. It is however recognised that most of the studies have methodological limitations. Therefore RAC agrees with the proposal from the DS that glass microfibres of representative composition warrant classification as Carc. 2 with hazard statement H350: "May cause cancer". The route of exposure inhalation shall also be added after the hazard statement code.

Comparison with the criteria for applying notes specific to fibres

The two existing entries in the CLP Regulation with index numbers 650-016-00-2 and 650-017-00-8 contained also notes A, Q, R and A, R (respectively) which are described as follows in Annex VI of the CLP Regulation:

Note A :

Without prejudice to Article 17(2), the name of the substance must appear on the label in the form of one of the designations given in Part 3 of Annex VI. In Part 3, use is sometimes made of a general description such as '... compounds' or '... salts'. In this case, the supplier is required to state on the label the correct name, due account being taken of section 1.1.1.4.

Note Q :

The classification as a carcinogen need not apply if it can be shown that the substance fulfils one of the following conditions:
— a short term biopersistence test by inhalation has shown that the fibres longer than 20 µm have a weighted half-life less than 10 days; or
— a short term biopersistence test by intratracheal instillation has shown that the fibres longer than 20 µm have a weighted half- life less than 40 days; or
— an appropriate intra-peritoneal test has shown no evidence of excess carcinogenicity; or
— absence of relevant pathogenicity or neoplastic changes in a suitable long term inhalation test.

Note R :

The classification as a carcinogen need not apply to fibres with a length weighted geometric mean diameter less two standard geometric errors greater than 6 µm.

RAC proposes to apply **note A** from Annex VI of the CLP Regulation, which states that without prejudice to Article 17(2), the name of the substance must appear on the label in the form of one of the designations given in Part 3. Table 3.1: List of harmonised classification and labelling of hazardous substances

RAC is of the opinion that the glass microfibres of representative composition should not be marked with **note R** from Annex VI of the CLP Regulation, which states that "*classification as a carcinogen need not apply to fibres with a length weighted aerodynamic geometric mean diameter less two standard geometric errors (LWGMD) greater than 6 µm*". The test method was published in Commission Regulation (EC) No 761/2009 (EC, 2009). The measurement method for the LWGMD under note R was created to characterise the fibre diameter of bulk substances or products containing MMMFs including Refractory Ceramic Fibres, man-made vitreous fibres (MMVF), crystalline and

polycrystalline fibres. The length weighting is a means of compensating for the effect on the diameter distribution caused by the breakage of long fibres when sampling or handling the material. Geometric statistics (geometric mean) are used to describe the size distribution of MMMF diameters, because their diameters usually approximate to log normal distributions (ECB, draft 4). RAC concluded that note R is a measure for diameter and not length. The methods of manufacture given in the name of the entry (rotary and flame attenuation) and the name itself 'microfibres' also discount continuous filaments and also would not generate fibres with diameters > 6 µm. Indeed, the typical methods of manufacturing processes reported in publicly available literature (i.e. mostly from industry) are flame attenuation and rotary process, which determine the diameter of the fibre. The ranges of nominal diameters produced for these microfibres are less than 3 microns for rotary blowing process and less than 2-4 microns for flame attenuation process. This means that the LWGMD is not applicable to glass microfibres.

RAC is also of the opinion that glass microfibres of representative composition should not be marked with **note Q**. Indeed, the experimental evidence shows biopersistence and excessive carcinogenicity which does not allow an exemption of the classification as a carcinogen.

Finally, with regards to the identity of the substance, it is stated that "additional individual elements may be present at low levels". These elements, although at low levels and dependent on the manufacturing process, may influence both the toxicity and the biopersistence of the glass microfibres. It is also stated in the substance identity that "the process list does not preclude innovation" because there may be other "fiberisation" technologies or methods not covered in the proposed naming (e.g. Fi-high speed F-Technology).

4.10 Toxicity for reproduction

No data.

4.11 Other effects

No data.

4.11.1 Non-human information

No data.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant for this dossier.

6 OTHER INFORMATION

Not relevant.

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8 ANNEXES

Discussions at the TC C&L:

Summary records – TC C&L November 2005 (doc ECBI/60/05 Rev. 3)

In **November 2005** a preliminary discussion took place.

Discussion of this substance was introduced by France, which reported that special purpose fibres were incorrectly regarded in the same Annex I entry as mineral wool. In fact they should be in the same entry as refractory ceramic fibres as a result of their known carcinogenicity. The French proposal was for a classification of special purpose fibres as Carc. Cat.2; R45.

Industry responded to their paper (Add 1). They argued that special purpose fibres fell into two broad sub-Groups one of which (E glass) should be classified as a category 2 carcinogen. However the second sub-Group (identified as fibres of which the type 475 is considered representative) did not have the same properties and should be considered as a category 3 carcinogen.

In the course of discussion, member states raised a number of concerns. France drew attention to the difficulty of inhalation studies as a valid test for eliminating concerns over the carcinogenicity of fibres. Germany pointed out the importance of IP studies. The United Kingdom asked for further information, particularly the arguments that observations of mesothelioma in hamsters were not relevant to humans.

Industry promised to provide further information, particularly the relationship between inhalation and IP studies. The Chair said the discussion would be taken up again at the next meeting.

Summary records – TC C&L Mars 2006 (doc ECBI/90/06 Rev. 8)

ECBI/10/05	F, classification proposal.
ECBI/10/05 Add. 1, 2,3,4	IND, respose to proposal

In **November 2005** a preliminary discussion took place and industry promised to provide further information on a number of issues.

Carcinogenicity

The Chair introduced this substance by reporting that industry said it preferred to keep the existing Annex 1 entry with the Carc Cat 3 classification. France was invited to react to the industry comments on their proposal.

France reported that it maintained the view that the existing classification was unsatisfactory. The fibres covered by the entry are persistent with a half-life similar to E glass. This suggested similar properties and it was appropriate to classify both special purpose fibres and E glass as a Carcinogen Category 2.

In responding to these comments Industry said the database on the substance had not changed since the original classification. There was no statistical difference in the frequency of adenocarcinomas and there was an absence of fibrosis. Bio-persistence was not a valid inclusion criterion for carcinogenicity; it had only been used in the past to enable exoneration. The only valid data were the complex inhalation studies which had been carried out prior to the 1977 classification decision.

During the subsequent discussion the United Kingdom indicated that they preferred keeping the original Carc. Cat 3 classification. However other Member States noted the confusion in relation to the description of the substance in the current entry which appeared to include E glass for which there was good evidence for Carc Cat 2. This led Germany and the Netherlands to suggest that a split entry might be appropriate. However they acknowledged there would be difficulties in developing a suitable characterisation of the substance.

Conclusion:

In drawing the discussion to a close the Chair suggested Member States needed to reflect on the issue. There appeared to be three possibilities; to maintain the status quo, to adopt the French proposal, or to develop split entries. Industry commented that the latter option would be extremely difficult to introduce.

Summary records – TC C&L October 2006 (doc ECBI/13/07 Rev. 2)

ECBI/10/05	F, classification proposal.
ECBI/10/05 Add. 1, 2, 3, 4	IND, response to proposal
ECBI/10/05 Add. 5	IND, summary of chemistry and key toxicological issues

In **November 2005** a preliminary discussion took place and industry promised to provide further information on a number of issues.

In **March 2006**, it was agreed to delete the Xi; R38 classification for both entries 650-016-00-2 (including CAS number 65997-17-3) and 650-017-00-8. The Chair suggested Member States needed to reflect on the carcinogenicity issue. There appeared to be three possibilities; to maintain the status quo, to adopt the French proposal, or to develop split entries. Industry commented that the latter option would be extremely difficult to introduce.*Carcinogenicity:*

ECB summarised the conclusions from the last meeting. Re-classification was needed for E-glass fibres. IND had sent additional information on ‘E-glass’ and ‘Type 475 special purpose fibres’ and wanted them to be considered as different. Epidemiology data did not warrant a Carc. Cat. 2 classification for the Type 475 fibres, according to IND. There was no significant fibrosis in the Cullen study, therefore no carcinogenicity classification warranted. A further paper was published the week prior the meeting and would be distributed to the TC C&L during the Follow-up period. The Type 475 special purpose fibres should be classified with Carc. Cat. 3, according to IND.

ECB said at the last meeting there were split opinions between Carc. Cat. 3 and Carc. Cat. 2. We had a discussion to split the fibres amongst 2 entries.

F commented on the bio-persistence and bio-availability. The two types of fibres had different composition. The ‘Type 475 special purpose fibres’ and ‘E-glass fibres’ had different dissolution rates. Both fibres could be grouped on this basis and no split entry was needed. The E-glass fibres induced fibrosis. Also very slight fibrosis was found with ‘Type 475 special purpose fibres’ at short exposure. For F this was enough evidence for Carc. Cat. 2, for both fibre categories.

NL asked said that they had looked at dissolution rate and then at fibrosis, but they did not see the relation between dissolution rates and the category.

IND said the dissolution rate is an interesting concept. When developed, nobody felt that this could be used for C&L purposes. It was an indication of a relative category of where the fibres belong. The difference between Carc. Cat. 2 and Carc, Cat. 3, however, must be determined by toxicological studies. In this case the inhalation study was negative. There was also not significant fibrosis. Therefore we need different categories for ‘Type 475 special purpose fibres’ and ‘E-glass fibres’.

UK agreed with IND that the two fibre types are different. Thus Carc. Cat. 3 for 'Type 475 special purpose fibres'. NL also agreed to this.

DE said there was a different potency between the fibres. However, also 'Type 475 special purpose fibres' could still be classified as Carc. Cat. 2. A practical problem was also how to present the classification in Annex I because both fibres had the same CAS number. F confirmed the CAS number covers many fibres.

ECB summarised the TC C&L agreed to classify the 'Type 475 special purpose fibres' in Cat. 3. IND was asked to provide the chemical identification for both entries in the Follow up procedure. The TC C&L agreed to classify the 'Type 475 special purpose fibres' in Carc. Cat. 3 and the E-glass fibres in Carc. Cat. 2, and the only remaining issue was then how to identify the substances in the two different entries.

IND confirmed that they would provide further information in the Follow up procedure.

F asked IND what the percentage of oxide was in the fibres. IND responded: greater than 18 % but close to the limit.

Conclusion:

The TC C&L agreed to classify 'Type 475 Special purpose fibres' with Carc. Cat. 3; R40 while 'E-glass fibres' would remain with the current Carc. Cat. 2; R49 classification.

Follow-up:

IND sent in ECBI/10/05 Add. 6 for identification of the substances to be covered by the two entries.

F proposed to define following four entries for fibres:

- To keep the current entries Index 650-017-00-8 and Index 650-016-00-2 as they are.

- To create one additional entry for E-fibres (with a new index number) and one additional entry for 475-fibres (which will differ from index 650-016-00-2 by the absence of nota Q).

Follow-up conclusion:

The definition of the new entries should be confirmed at the March 2007 meeting.

Follow-up III of TC C&L October 2006 (doc ECBI/09/07)

IND sent in ECBI/10/05 Add. 6 for identification of the substances to be covered by the two entries.

Member States were invited to react in case they did not agree with the entries as identified.

FR: The current index 650-017-00-8 also covers refractory ceramic fibres (RCF) and should therefore not be restricted to E-fibres.

Besides, the current index 650-016-00-2 which is classified Carc. Cat. 3; R40 and could apply by default to 475-type fibres, is specific because of nota Q which allows exemption of the carcinogenic classification under certain circumstances.

For these reasons, we propose to have the following entries:

- To keep the current entries Index 650-017-00-8 and Index 650-016-00-2 as they are.

- To create one additional entry for E-fibres (with a new index number) and one additional entry for 475-fibres (which will differ from index 650-016-00-2 by the absence of nota Q).

Besides, the chemical composition of the glass may not be sufficient to characterise appropriately the entries. To our knowledge, E-glass may also be used in other type of glass fibres than special purpose fibres, such as continuous glass filaments for example. Therefore, an appropriate way to identify the entries could be to specify both composition and size and to limit the entries to fibres with a mean diameter of less than 3 µm.

IND sent documents ECBI/10/05 Add. 8 parts I, II and III. The values of the type 475 fibres are corrected in correspondence with the table of document 10/05 Add. 8 part II.

MS were asked to react in written in case they do not agree to the new IND proposal prior 31 August 2007. In case no reactions no further detailed discussion is foreseen to take place at the September meeting, but the entry as defined here can be considered confirmed.

No further comments were received.

Final Conclusion:

TC C&L has then confirmed the entry as written here, and there will be no further discussion.

After FUII:

ECB: The CAS No 65997-17-3 is coupled to EC No 266-046-0 with the substance name *Glass, oxide, chemicals* and a description starting with '"This category encompasses the various chemical substances manufactured in the production of inorganic glasses……..". Whether the CAS and EC Numbers should be assigned to the more specified entry *Type 475 Special purpose fibres* still has to be decided before this entry is included in the next ATP.