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**

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Part A.

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		

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	'475' type -glass fibres: • 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	E-glass fibres: • 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			475-glass fibres: • 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 x 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 x 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.

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.

7 REFERENCES

Achard Ellouk S, Jaurand MC. Review of animal / *in vitro* data on biological effects of man-made fibres. Environ Health Perspect 1994; 102 (suppl 2), 47-63

AFSSET, Les fibres minérales artificielles : Evaluation de l'exposition de la population générale et des travailleurs ; « Rapport final relatif aux fibres céramiques réfractaires et aux fibres de verre à usage special »; Saisine n° « 2004-012 » ; janvier 2007.

ATSDR. (2004). Toxicological profile for Synthetic Vitreous Fibres (Atlanta, Georgia, U.S. department of health and human services, Public Health Service, Agency for Toxic Substances and Disease Registry).

Aufderheide M et al. Differences in the biological effects of crocidolite asbestos and two glass fibres on epithelial lung cells. Exp Toxicol Pathol. 1994 Apr;45(8):467-72

Bellmann B, Muhle H, Creutzenberg O et al. Calibration study on subchronic inhalation toxicity of man-made vitreous fibres in rats. Inhalation Toxicology 2003; 15:1147-1177

Bernstein D.M. Special-Purpose Fiber Type 475-Toxicological Assessment. Inhalation Toxicology 2007; 19:149–159.

Blake T et al. Effect of fibre length on glass microfibre cytotoxicity. J Toxicol Environ Health A. 1998 Jun 26;54(4):243-59

Brown DM et al. Effect of coating with lung lining fluid on the ability of fibres to produce a respiratory burst in rat alveolar macrophages. Toxicol in Vitro 1998; 12(1):15-24

Castranova V et al. In vitro effects of large and small glass fibres on rat alveolar macrophages. J Toxicol Environ Health. 1996 Nov;49(4):357-69

Cullen RT et al. Pathogenicity of a special-purpose glass microfibre (E glass) relative to another glass microfibre and amosite asbestos. Inhal Toxicol. 2000 ;12(10):959-77

Cullen RT et al. Short-term inhalation and in vitro tests as predictors of fibre pathogenicity. Environ Health Perspect. 1997 Sep;105 Suppl 5:1235-40

Davis JMG et al. A comparison of methods of determining and predicting the pathogenicity of mineral fibres. Inhalation Toxicology 1996; 8:747-770

Donaldson K et al. Bromo-deoxyuridine (BRDU) uptake in the lungs of rats inhaling amosite asbestos or vitreous fibres at equal airborne fibre concentrations. Exp Toxicol Pathol 1995; 47(2-3):207-11

Eates W et al. Estimating rock and slag wool fibre dissolution rate from composition. InhalationToxicology 2000;12:1127-1139

Feron VJ et al. Pulmonary response of hamsters to fibrous glass: chronic effects of repeated intratracheal instillation with or without benzo[a]pyrene. Carcinogenesis. 1985 Oct;6(10):1495-9

Fisher CE et al. Release of TNF-alpha in response to SiC fibres: differential effects in rodent and human primary macrophages, and in macrophage-like cell lines. Toxicol In Vitro. 2000;14(1):25-31

Fraire AE et al. Effect of fibrous glass on rat pleural mesothelium. Histopathologic observations. Am J Respir Crit Care Med. 1994 Aug;150(2):521-7

Gao HG et al. Morphological transformation induced by glass fibres in BALB-c-3T3 cells. Teratog Carcinog Mutagen 1995; 15(2):63-71

Goldstein et al. Changes produced by the inhalation of glass fibre in non-human primates.). In: Biological effects of a man-made mineral fibres (Proceedings of a WHO/IARC conference), vol. 2, Copenhagen, WHO, 1984, pp 273-285

Hansen K, Mossman BT. Generation of superoxide (O2-.) from alveolar macrophages exposed to asbestiform and nonfibrous particles. Cancer Res. 1987, 15;47(6):1681-6.

Hart GA et al. In vitro cytotoxicity of asbestos and man-made vitreous fibres: roles of fibre length, diameter and composition. Carcinogenesis. 1994 May;15(5):971-7

Hesterberg TW et al. Role of phagocytosis in Syrian hamster cell transformation and cytogenetic effects induced by asbestos and short and long glass fibres. Cancer Res. 1986;46(11):5795-802.

Hesterberg TW et al. Biopersistence of synthetic vitreous fibres and amosite asbestos in the rat lung following inhalation. Toxicol Appl Pharmacol 1998; 151(2):262-75

Hesterberg TW et al. Chronic Inhalation Study of Fibre Glass and Amosite Asbestos in Hamsters: Twelve-month Preliminary Results. Environmental Health Perspectives 1997; 105, Suppl 5; 1223-9

Hesterberg TW, Barrett JC. Dependence of asbestos- and mineral dust-induced transformation of mammalian cells in culture on fibre dimension. Cancer Res. 1984;44(5):2170-80.

Hutten IM. Handbook of Nonwoven Filter Media. 13 Feb 2007. Elsevier Science, ISBN: 978-1-85617-441-1.

IARC. Man-made vitreous fibres. IARC monographs on the evaluation of the carcinogenic risks to humans. Vol 81, 2002. IARC, Lyon, France

INSERM. Effets sur la santé des fibres de substitution à l'amiante. Expertise collective INSERM, Paris, 1999

Jaurand MC. Mechanisms of fibre-induced genotoxicity. Environ Health Perspect 1997; 105 (suppl 5), 1073-84

John Mansville website. Accessed on 05/02/2014 (http://www.jm.com/en/manufacturers-solutions/fibers/microfiber/).

Johnson NF and Jaramillo RJ. P53, Cip1, and Gadd153 Expression following Treatment of A549 Cells with Natural and Man-made Vitreous Fibres. Environmental Health Perspectives 1997;105, Suppl. 5: 1143-45

Koshi K et al. Cell toxicity, hemolytic action and clastogenic activity of asbestos and its substitutes. Ind Health. 1991;29(2):37-56

Le Bouffant L et al. Experimental study on long-term effects of inhaled MMMF on the lungs of rats. Ann Occup Hyg. 1987;31(4B):765-90

Marchand JL et al. Laryngeal and hypopharyngeal cancer and occupational exposure to asbestos and man-made vitreous fibres: results of a case-control study. Am J Ind Med. 2000 Jun;37(6):581-9

Marsh GM et al. Historical cohort study of US man-made vitreous fibre production workers: I. 1992 fibreglass cohort follow-up: initial findings. J Occup Environ Med. 2001 Sep;43(9):741-56

McConnell EE et al. A comparative study of the fibrogenic and carcinogenic effects of UICC Canadian chrysotile B asbestos and glass microfibre (JM100). In: Biological effects of a man-made mineral fibres (Proceedings of a WHO/IARC conference), vol. 2, Copenhagen, WHO, 1984, pp 234-252

McConnell EE et al. Studies on the inhalation toxicology of two fibreglasses and amosite asbestos in the Syrian golden hamster. Part II. Results of chronic exposure. Inhal Toxicol. 1999 Sep;11(9):785-835

Mikalsen SO et al. Morphological transformation of Syrian hamster embryo cells induced by mineral fibres and the alleged enhancement of benzo[a]pyrene. Carcinogenesis. 1988 Jun;9(6):891-9

Miller BG et al. Influence of fibre length, dissolution and biopersistence on the production of mesothelioma in the rat peritoneal cavity. Ann Occup Hyg. 1999b Apr;43(3):155-66

Miller BG et al. Influence of characteristics of inhaled fibres on development of tumours in the rat lung. Ann Occup Hyg. 1999a Apr;43(3):167-79

Mohr U, Pott F, Vonnahme FJ. Morphological aspects of mesotheliomas after intratracheal instillations of fibrous dusts in Syrian golden hamsters. Exp Pathol. 1984;26(3):179-83

Monchaux G et al. Mesotheliomas in rats following inoculation with acid-leached chrysotile asbestos and other mineral fibres. Carcinogenesis. 1981;2(3):229-36

Moorman WJ et al. Chronic inhalation toxicology of fibrous glass in rats and monkeys. Ann Occup Hyg 1988; 32(suppl1): 757-67

Mossman BT, Sesko AM. In vitro assays to predict the pathogenicity of mineral fibres. Toxicology. 1990 Jan-Feb;60(1-2):53-61

Muhle H et al. Inhalation and injection experiments in rats to test the carcinogenicity of MMMF. Ann Occup Hyg. 1987;31(4B):755-64

Ong T et al. Induction of micronucleated and multinucleated cells by man-made fibres in vitro in mammalian cells. J Toxicol Environ Health. 1997 Mar;50(4):409-14

Pico, D., Wilm, C., Seide, G., Gries, T., Kleinholz, R. and Tiesler, H. (2012) Ullman's Encyclopedia of Industrial Chemistry – Chapter Fibres. Glass Fibers. Wiley-VCH Verlag GmbH & Co., Weinheim, Germany, 2012.

Pott F, Friedrichs KH, Huth F. [Results of animal experiments concerning the carcinogenic effect of fibrous dusts and their interpretation with regard to the carcinogenesis in humans (author's transl)] Zentralbl Bakteriol [Orig B]. 1976 Aug;162(5-6):467-505

Pott F et al. Animal experiments with chemically treated fibres. Ann Occup Hyg 1988;32:353-359

Pott F et al. New results from implantation experiments with mineral fibres. In: Biological effects of a man-made mineral fibres (Proceedings of a WHO/IARC conference), vol. 2, Copenhagen, WHO, 1984, pp 286-302

Pott F et al. Lung carcinomas and mesotheliomas following intratracheal instillation of glass fibres and asbestos. In: Proceedings of the Vith International Pneumoconiosis Conference, Bochum, Federal Republic of Germany, 20-23 September 1983, vol. 2, Geneva, International Labour Office, 1984, pp. 746-756

Pott F et al. Carcinogenicity studies on fibres, metal compounds, and some other dusts in rats. Exp Pathol. 1987;32(3):129-52

Pott F et al. Animal experiments with chemically treated fibres. Ann Occup Hyg, 1988;32(suppl 1):353-359

Pott F et al. Carcinogenicity studies on natural and man-made fibres with the intraperitoneal test in rats. IARC Sci Publ. 1989;(90):173-9

Pott F et al. Tumours by the intraperitoneal and intrapleural routes and their significance for the classification of mineral fibres. In: Brown RC, Hoskins JA & Johnson NF, eds, Mechanism in Fibre Carcinogenesis (NATO ASI Series 223), New York, Plenum Press, 1991, pp. 547-565

REACH registration dossiers from the REACH dissemination database (available through http://echa.europa.eu/web/guest/home).

Searl A et al. Biopersistence and durability of nine mineral fibre types in rat lungs over 12 months. Ann Occup Hyg. 1999 Apr;43(3):143-53

Smith DM et al. Long-term health effects in hamsters and rats exposed chronically to man-made vitreous fibres. Ann Occup Hyg. 1987;31(4B):731-54

Wagner JC et al. Animal experiment with MM(V)F – Effects of inhalation and intrapleural inoculation in rats. In: Biological Effects of Man-made Mineral Fibres (Proceedings of a WHO/IARC Conference) vol. 2, Copenhagen, WHO, 1984, pp209-233

Wagner JC et al. Studies of the carcinogenic effects of fibre glass of different diameters following intrapleural inoculation in experimental animals. In: LeVee WN & Schulte PA, eds, Occupational Exposure to Fibrous Glass (DHEW Publ. No. (NIOSH) 76-151, NTIS Publ. No. PB-258869), Cincinnati, OH, National Institute for Occupational Safety and Health, pp. 193-204

Ye J et al. Critical role of glass fibre length in TNF-alpha production and transcription factor activation in macrophages. Am J Physiol: Lung Cell Mol Physiol 1999; 20(3):L426-34

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.