Interpretation Memo: Assessing the carcinogenicity hazard of vitreous fibers

The Cradle to Cradle Certified Material Health Assessment Methodology (MHAM) lists both GHS categorization (i.e. by the European Chemicals Agency (ECHA) under the European regulation for the classification, packaging and labelling of dangerous substances (CLP)) and categorization by the German MAK commission among the authoritative sources that may be used in determining the carcinogenicity hazard rating of a substance. The MAK commission categorizes all vitreous fibers as presumed carcinogens while ECHA has granted exemptions to certain fiber types under Note Q or R in the CLP. As a result, there is potential for assessors to assign conflicting hazard ratings to materials qualifying for the Note Q or R exemption. Given this conflict, C2CPII has developed an interpretation that clarifies which classification scheme takes precedence, ensuring consistent assessment of vitreous fibers throughout the program.

Background

C2C Certified Carcinogenicity hazard rating criteria

The MHAM states the following regarding the assignment of hazard ratings for the carcinogenicity endpoint:

> *In order for a chemical to be rated RED for carcinogenicity, it is either known, presumed, or suspected to be a carcinogen based on human epidemiologic or animal studies. The YELLOW rating for carcinogenicity is reserved for chemical substances that, based on experimental evidence, cannot be classified as a carcinogen or non-carcinogen due to a lack of evidence, equivocal evidence based on experimental structure, or conflicting evidence. In order for carcinogenicity to be rated GREEN, the chemical in question is not suspected to be a human carcinogen based on evidence from long-term studies.*
>
> *There are several existing classification systems that align with this rating scheme including the Threshold Limit Value (TLV), International Agency for Research on Cancer (IARC), maximum workplace concentration (MAK), and GHS. Based on these classification systems, if a chemical is listed within these publications, a hazard rating can be given for the carcinogenicity endpoint as summarized in Table 5 below.*

Table 5 Rating Criteria for Carcinogenicity

Green	Yellow	Red	Grey
Not classified as GHS category 1A, 1B, or 2. Not a known, presumed or suspected carcinogen. Negative long-term cancer studies. Listed as: TLV A5, IARC 4	Not classified as GHS category 1A, 1B, or 2. Limited, marginal, equivocal or conflicting evidence of carcinogenicity. Listed as: MAK III 3A, 4, 5	Classified as GHS category 1A, 1B, or 2. Known, presumed or suspected carcinogen. Listed as: MAK III 1, 2, 3B IARC Group 1, 2A, 2B TLV A1, A2, A3 GHS Category 1A, 1B, 2 H350: May cause cancer H351: Suspected of causing cancer	No data available for classification. Listed as: IARC Group 3 TLV A4

The MHAM further states that the strength and weight of evidence must be considered when determining whether a chemical is classifiable as a carcinogen.

Classification of vitreous fibers following ECHA

Under CLP, vitreous fibers are subdivided into two distinct types based on their chemical composition. The ECHA Risk Assessment Commission (RAC) has developed harmonized classifications for these two vitreous fiber types as either GHS category 2 or GHS category 1B for carcinogenicity (see table below).

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

However, in the case of the first type (vitreous fibres with alkaline oxide and alkali earth oxide (Na2O+K2O+CaO+MgO+BaO) content greater than 18 % by weight), notes Q and R, which

were added via Commission Directive 97/69/EC, provide an exemption from classification for substances meeting certain requirements:

> *Note 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.*
>
> *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.*

Following ECHA's categorization under CLP, vitreous fibres would receive a **YELLOW** rating for carcinogenicity if they can be shown to meet one or more of the conditions stipulated by Note Q or R (see above) and a RED hazard rating for carcinogenicity otherwise. All other vitreous fibers would receive a RED hazard rating for carcinogenicity following ECHA's classification.

Classification of vitreous fibers following MAK

In the 'List of MAK and BAT Values 2012' prepared by the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, all glass fibers are assigned to the carcinogenicity hazard category 2 (*Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can contribute to cancer risk. Limited data from animal studies can be supported by evidence that the substance causes cancer by a mode of action that is relevant to man and by results of in vitro tests and short-term animal studies*). The commission considered the impact of durability on carcinogenicity potential and concluded:

> *From the results of animal studies with durable and non-durable fibres it is concluded that durability in the biological system has a considerable effect on the carcinogenicity of fibres. At present, however, it is not possible to define the degree of durability necessary for carcinogenic activity or to state to what extent the durability determines the carcinogenic potency of the fibres. Gypsum and wollastonite, e. g., dissolve in the organism within a period of some days to a few weeks and show no signs of carcinogenic effects even after intraperitoneal administration. Thus it must be concluded*

> *that it is not possible at present to formulate a precise scientific definition of the factors which determine the carcinogenicity of fibres.*

Since all vitreous fibers are assigned to the carcinogenicity hazard category 2, they would receive a **RED** hazard rating for carcinogenicity if following the MAK categorization.

Classification of vitreous fibers following IARC

Vitreous fibers used to be categorized as 'possible human carcinogen' (Group 2B) by IARC, which would have led to a RED hazard rating following this categorization. However, in 2001, the Monographs working group re-evaluated the categorization based on studies of newer products that disappear from body tissues much more rapidly and concluded:

> *The Monographs working group concluded that only the more biopersistent materials remain classified by IARC as possible human carcinogens (Group 2B). These include refractory ceramic fibres, which are used industrially as insulation in high-temperature environments such as blast furnaces, and certain special-purpose glass wools not used as insulating materials. In contrast, the more commonly used vitreous fibre wools including insulation glass wool, rock (stone) wool and slag wool are now considered not classifiable as to carcinogenicity to humans (Group 3).*

Thus, following the IARC categorization, the more commonly used vitreous fiber types used in insulation today (including insulation glass wool, rock (stone) wool, and slag wool) would receive a **GREY** hazard rating for carcinogenicity, which in the absence of other RED or GREY risk flags would yield a 'c' risk rating for the fibers.

General interpretation (to be integrated into the C2C Certified Material Health Assessment Methodology)

If a harmonized classification for a chemical substance has been developed by ECHA through the Harmonised classification and labelling process (CLH) and is listed in Annex VI to the CLP Regulation, this classification must be followed in the derivation of a hazard rating for the substance in accordance with the Cradle to Cradle Certified Material Health Assessment Methodology. The harmonized GHS classification approach by ECHA takes precedence over other authoritative sources.

Case-specific interpretation

The carcinogenicity endpoint of vitreous fibers shall be assessed following the categorization and methods developed and published by ECHA under the CLP regulation under Note Q or R. In particular, vitreous fibres with alkaline oxide and alkali earth oxide content greater than 18 % by weight will receive a YELLOW hazard rating for carcinogenicity if one of the following conditions is met for the specific fiber composition[1] being assessed:

- 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.

Furthermore, vitreous fibers of any chemical composition will receive a YELLOW hazard rating for carcinogenicity if they have a length-weighted geometric mean diameter less two standard geometric errors greater than 6 µm.

[1] Biopersistence and/or carcinogenicity test results must be from a vitreous fiber of similar chemical composition and manufactured with the same process as the assessed vitreous fiber. Similarity in chemical composition of the assessed fiber from each facility at which it is produced with the tested fiber must be confirmed annually to maintain the YELLOW hazard rating for this endpoint. Alkaline/alkali earth oxide content (Na_2O, K_2O, CaO, MgO, MaO) must be at least 18% for the assessed fiber and the content of each alkaline/alkali earth oxide contained may not differ by more than 5% from the sample(s) for which the biopersistence and/or carcinogenicity was confirmed in according to CLP Note Q or R. Furthermore, the SiO_2 concentration may be no greater than, and the Al_2O_3 and CaO+MgO concentrations may be no less than those of the sample(s) for which the biopersistence and/or carcinogenicity was confirmed in according to CLP Note Q or R.

Any vitreous fiber not meeting one or more of these conditions must be assigned a RED hazard rating for carcinogenicity.

Rationale

ECHA's categorization approach of vitreous fibers was chosen over MAK's for the following reasons:

- The MAK commission supports the consensus that certain mineral fibers show no signs of carcinogenic effects and are not of concern, but does not provide guidelines for determining when this may be the case, opting instead for a global categorization.
- ECHA's more nuanced approach towards the carcinogenicity categorization of vitreous fibers aligns with the positions taken by IARC and the US National Toxicology Program.
- As the body administering chemical regulation and classification at the European level, ECHA is viewed as having a higher level of authority compared to the MAK commission, which advises the German governments, parliaments, and public authorities on chemical health protection issues at the national level, but is not itself responsible for administering regulation at the national or international level[2].
- Under the harmonised classification and labelling process administered by ECHA, which the interpretation is based on, member state competent authorities[3] may propose revisions of existing harmonised entries for any substance that is under the scope of the CLP Regulation. Thus, a mechanism exists to review and update this categorization approach should it be found to be inadequate. While C2CPII is currently not aware of any such efforts, our interpretation would follow any revisions to ECHA's harmonized classification approach on this matter should they be proposed and implemented.

[2] http://www.dfg.de/en/dfg_profile/statutory_bodies/senate/health_hazards/index.html
[3] Including some advised by the German MAK commission, such as the German ministry for the environment and the ministry of labor