Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report

Silicon dioxide Kieselguhr

Product-type 18
(insecticides, acaricides and products to control other arthropods)

November 2016

France

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

In Regulation (EU) No 1062/2014 the active substance is referred to as "Silicium dioxide (Silicium dioxide Kieselguhr)" (Entry number 831 in Annex II, Part 1). For the approval, the substance is renamed into silicon dioxide Kieselguhr. Diatomaceous Earth is also used as synonym.

This Assessment Report has been established as a result of the evaluation of the active substance silicon dioxide Kieselguhr, CAS n°. 61790-53-2, as product-type 18 (Insecticides, Acaricides and products to control other arthropods), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products, with a view to the possible approval of this substance.

Silicon dioxide Kieselguhr (CAS n°. 61790-53-2) was notified as an existing active substance, initially by Dr. Schaette AG for product-type 18, then by Biofa AG. Data on the representative product were submitted by the substance and biocidal product manufacturer Biofa AG.

Commission Regulation (EC) No 1062/2014 of 4 August 2014[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

On the 15th June 2009, the French competent authority received a dossier from Dr. Schaette AG. The Raporteur Member State accepted the dossier as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of this dossier on the 31st December 2009.

On December 2015, the evaluating Competent Authority submitted to European Chemical Agency (ECHA), hereafter referred to as the Agency, and the applicant a copy of the evaluation report, hereafter referred to as the Competent Authority Report.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the "Agency" (ECHA). Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

1.2. Purpose of the assessment report

The aim of Assessment Report is to support a decision on the approval of silicon dioxide Kieselguhr for product-type 18, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 18 that contain silicon dioxide Kieselguhr. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site, shall be taken into account.

However, where conclusions of this assessment report are based on data protected under

[1] COMMISSION DELEGATED REGULATION (EU) No 1062/2014 of 4 August 2014 on the work programme for the systematic examination of all existing active substances contained in biocidal products referred to in Regulation (EU) No 528/2012 of the European Parliament and of the Council. OJ L 294, 10.10.2014, p. 1

the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity

Table 2.1.1-1: Identification of silicon dioxide Kieselguhr

CAS-No.	**61790-53-2**
EINECS-No.	612-383-7
Other No. (CIPAC, ELINCS)	CIPAC : 647
IUPAC Name	No IUPAC name
Common name, synonym	Common name: Silicon dioxide Kieselguhr Synonym: Kieselguhr, , Diatomaceous earth
Molecular formula	Silicon dioxide Kieselguhr is composed of a mixture of inorganic oxides
Structural characteristics	Silicon dioxide Kieselguhr is composed of a mixture of inorganic oxides. Particle size distribution: L50D > 7 µm; Specific surface area : 30 - 45 m²/g
Purity	As it is an UVCB[2]: purity of silicon dioxide Kieselguhr 100%
Molecular weight (g/mol)	Not relevant

Initially, the name of the active substance in the review program was Silicium dioxide (Silicium dioxide Kieselguhr), however, silicium is the French word for silicon. The name was changed to the English version. There is no modification of the active substance definition.

Table: 2.1.1-2: Identification of the major component of active substance: silicon dioxide

CAS-No.	7631-86-9
EINECS-No.	Not allocated
Other No. (CIPAC, ELINCS	Not allocated
IUPAC Name / chemical name	Amorphous silicon dioxide
Molecular formula	SiO_2 Silicon dioxide Kieselguhr contains SiO_2 in an amorphous form. Molecules build up tetrahedric room-net structures (SiO_4), which are connected through siloxan-bridges (Si-O-Si).
Content in silicon dioxide Kieselguhr	Minimum content of silicon dioxide in silicon dioxide Kieselguhr : 70%

[2] UVCB: Unknown or Variable composition Complex reaction product or.Biological origin ...

Structural formula	XXXX
Molecular weight (g/mol)	60.08

Silicon dioxide Kieselguhr is composed of the skeletal remains of diatoms, a microscopic form of alga. The diatom shells and fragments can range in size from 1-1000 µm, however the average size is between 50-100 µm depending on species and growth conditions. Depending on species the shape of the shells can also vary, but are frequently boat shaped or wheel like in appearance.

This pattern is to be compared with other structures found for synthetic amorphous silicon dioxide which looks like random aggregated mass. Thus Rapporteur Member State (RMS) is of the opinion that no read across based on physico-chemical data can be established between natural and synthetic amorphous silica.

The most notable character of these shells or minute particles is that they are permeated by pores forming a delicate lace like structure. The pores in the shells are very small (1-3 µm) in diameter and often many species one or two finer networks of secondary pores (<0.5µm and < 0.05 µm) within the primary pores. That mean that silicon dioxide Kieselguhr should be considered as a nanostructured material.

Analyses of electron microscopies of silicon dioxide/ Kieselguhr silicon dioxide Kieselguhr are submitted for the purpose of this dossier and are available in the confidential part of the dossier. Particle size distribution on several batches indicates that most of the particles are in the range 2-19 µm and that there is no particle below 100 nm. Specific surface area was measured on several batches for a value 34.6-43.8 m²/g.

According to the nanomaterial definition of the commission recommendation 2011/696/EU[3], the silicon dioxide Kieselguhr is a nanostructured material due to its specific surface area (>60 m2/cm3).
However, according to the nanomaterial definition of the biocidal products regulation (EU) No 528/2012, the silicon dioxide Kieselguhr is not a nanostructured material as the specific surface area criteria is not taken into account in the BPR definition.

Silicon dioxide Kieselguhr has a specified purity of 100 % w/w (1000 g/kg).
The content of silicon dioxide in silicon dioxide Kieselguhr can be used as a marker and is set at 70 % w/w.

A relevant impurity was identified: crystalline silica with a maximum content of 0.1 % w/w.
The identity of other ingredients is confidential.

[3] Commission recommendation of 18 October 2011 on the definition of nanomaterial, OJ L 275/38 20.10.2011.

2.1.2. Physico-Chemical Properties

The active substance silicon dioxide Kieselguhr is a white powder. Its melting point is above 1400°C; its boiling point is above. 2200°C. The tap density is 0.32 g/mL.

Silicon dioxide particle is not soluble in water or organic solvents. However, it forms stable suspensions.

Partition coefficient - n-octanol/water is not relevant for silicon dioxide.

Silicon dioxide Kieselguhr is neither flammable nor auto-flammable nor degradable. Silicon dioxide Kieselguhr has no oxidizing or explosive properties and shows no re-activity towards its container material (polyethylene high density (PE/HD) foil as inner package surrounded by a cardbox as outer package).

2.1.3. Methods of Analysis

ICP-OES has been provided by the applicant as analytical method of the substance, which was deemed quantitatively sufficient.

An X-ray analysis has been provided for the determination of the relevant impurity crystalline silica in the active substance. However, no validation data is available in the study. As the method is derived from a NIOSH method, the proposed method is considered acceptable nevertheless validation data are needed for confirmation and to set a limit of quantification (LOQ).

Identification of the biocidal product

The representative product is 100% of the active substance, i.e. 100% of silicon dioxide Kieselguhr.

Trade name	InsectoSec	
Manufacturer's development code No(s)	No manufacturer's development code number is available for the biocidal product.	
Ingredient of preparation	**Function**	**Content (purity)**
Silicon dioxide Kieselguhr	Active substance	100%
Physical state of preparation	Dustable powder.	

2.1.4. Intended Uses and Efficacy

Field of use: Insecticides, Acaricides and Products to Control Other Arthropods (PT18)

Function: the representative biocidal product INSECTOSEC is to be used:

- by professional operators for the control of poultry red mites in poultry pens and for the control of arthropods in food and feed processing industry or storage facilities.

- by non-professionals for the control of arthropods in private households by crack and crevice treatment and by pouring dust barriers.

The representative product INSECTOSEC containing 100 % of the active substance is a dustable powder which is applied as dry dust with a handheld bellow, electrostatic dusters and dusting guns with compressed air (against poultry mites), by a dust barrier (against Black ant, Silverfish, Wood louse) and by surface treatment (against cat fleas).

In order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.5. Mode of action

The mode of action of natural silicon dioxide Kieselguhr is assumed to be the same as surface-treated amorphous silica.

Although the mechanism of biocidal action of surface-treated amorphous silica is currently not clear, "*The Manual of Decisions for Implementation of Directive 98/8/EC Concerning the Placing on the Market of Biocidal Products*"[4] updated on 10th July 2008 states in its section 2.3.3 that product containing amorphous silica in a water base *"seems to act through absorption of the lipid layer covering the insect's chitin protection, which then leads to desiccation and death of the target organism".* By destroying the natural water barrier, the waxy layer of the cuticle and hence disrupting the functioning of the water preservation mechanism, silica interferes with physiological processes.

2.1.6. Effects on target organisms

Several laboratory studies were submitted with the active substance and the representative product. Results demonstrated sufficient efficacy against the target species in the following conditions

- Against adult fleas (*Ctenocephalides felis*) at the application rate of 10 g/m^2 on carpets.
- To prevent the introduction of adult Black ants (*Lasius niger*), Wood Lice (*Porcellio scaber*) and Silverfishes (*Lepisma saccharina*) in food and feed processing industry facilities, private households, etc. using a dust barrier (0.5-2 cm width and app. 2 mm height) of InsectoSec (= 100 % of silicon dioxide kieselguhr) corresponding to a dose of 5 g/m.
- To control adult and larvae poultry red mites (*Dermanyssus gallinae*) at the application rate of 50 g/m^2 during 28 days with 3 applications at D0, D7 and D21.

As effectiveness on ants was of 80 %, further studies must be provided at product authorisation stage in order to confirm the effectiveness of silicon dioxide Kieselguhr on this target organism.

Furthermore, concerning fleas, it is to be noted that an irrelevant stage namely adult cat fleas has been tested (and claimed). This stage stays most of the time on the pet contrary to larvae. Relevance of claimed stage according to the intended uses should be checked at product authorization level.

Even if sufficient level of efficacy has been shown in laboratory for the claimed organisms, test conditions are not representative enough of real in-use conditions (excepted for poultry red mites). Field tests will need to be provided at product authorization stage for all claimed target organisms.

2.1.7. Resistance

Resistance *per se*, i.e. the ability of a given population to withstand a poison that was effectively lethal to earlier generations of the species, has not been observed for silicon dioxide Kieselguhr. Furthermore, on the basis of the physical type and non-specificity of

[4] At the time of the submission of the dossier and the assessment of the efficacy data, decisions reported in the Manual of Decisions applied. Although this guidance is no longer applicable under BPR, this statement regarding the active substance is still valid.

the mode of action, resistance is unlikely to develop.

2.1.8. Classification and Labelling

There is no harmonised classification and labelling of the active substance. A classification and hazard statement according to the Regulation 1272/2008 is proposed as follows:

Classification according to Regulation (EC) No 1272/2008 (CLP)		
Class of danger	STOT RE 2-	Warning
Hazard statement	H373-	May cause damage to organs (lungs) through prolonged or repeated exposure
Note	EUH 066-	Repeated exposure may cause skin dryness or cracking

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification and effects assessment

The substance, under consideration for this assessment and relevant for the claimed application, is a natural silicon dioxide kieselguhr, also named Kieselguhr (CAS No 61790-53-2), which has been proved to be amorphous silica by a X-ray analysis.

The silicon dioxide kieselguhr is not a nanomaterial according to BPR; if nano form of the active substance exists, the nanomaterial properties have not been taken into account in the following toxicological assessment and hence are not covered by the conclusions reached on the active substance.

Read-across between the different types of amorphous silica

Initially, no toxicological study was performed with the notified silicon dioxide Kieselguhr. The dossier was accepted by the RMS based on the following arguments:

1) Exposure considerations

Silicon dioxide Kieselguhr occurs ubiquitously in the environment. Indeed, silicon dioxide and silicates correspond to about 25% of the earth’s crust and are present in practically all plants, animals and in natural waters. Furthermore silicon dioxide Kieselguhr is used in a wide variety of applications (including filter, anti-cacking, laboratory absorbents, carrier for pesticides…).

2) Toxicological data available with substances other than the notified active substance

The toxicological endpoints were filled by the applicant with data on substances other than the notified active substance, such as synthetic amorphous silica, silicon dioxide Kieselguhr or mixture of silicon dioxide Kieselguhr and synthetic amorphous silica.

The read-across with studies performed on silicon dioxide Kieselguhr was accepted by the RMS based on the same nature of the substance considered and on the purity of silicon dioxide in the tested materials, highest than the specification for the notified silicon dioxide Kieselguhr.

The read-across with studies performed on mixture of silicon dioxide Kieselguhr and synthetic amorphous silica was also accepted given the high content of silicon dioxide Kieselguhr in the tested material and since it has been considered that the presence of synthetic amorphous silica does not impact the toxicity of the mixture for the endpoints taken into account.

For the read-across between synthetic amorphous silica and the notified natural silica (silicon dioxide Kieselguhr), RMS is of the opinion that no read across can be established between these two types of silica based on a comparison of particles structure. Indeed, silicon dioxide Kieselguhr is skeletons of algae whereas synthetic amorphous silica is random aggregated mass.

However, a low oral absorption potential is expected for natural and synthetic amorphous silica based on their insolubility in water and the absence of irritating potential which could enhance absorption. Furthermore, no adverse effects were found in studies performed with natural and synthetic amorphous silica at doses up to over 1000 mg/kg bw/day for durations between 2 weeks and 2 years. Finally, silicon dioxide is used as a food additive and is classified as "Generally Recognised as Safe" (GRAS) by the US Food and Drug Administration (FDA). Therefore all these above arguments support that data from synthetic silica can be used as supportive information to estimate systemic toxicity after oral administration of natural silica.

The main identified concerns for amorphous silica were local toxicity by inhalation and genotoxicity. In this context, a 90 day repeated-dose study by inhalation and an in vivo Comet assay performed with the notified silicon dioxide Kieselguhr were required by the RMS.
To conclude, considering the above, the RMS considers the dossier sufficient with the additional required toxicological data (genotoxicity and inhalation studies). In addition, considerations have been given to minimise testing on vertebrate animals or to avoid unnecessary suffering of experimental animals.

Toxicokinetics

No study on oral, dermal or inhalation absorption is available.
No systemic effect has been identified and only a risk assessment for local effects is performed.
Absorption values are therefore not required.

Acute toxicity

No study was performed with the notified silicon dioxide Kieselguhr. Studies were submitted with Dryacide powder (containing > 90 % silicon dioxide Kieselguhr, < 10 % silica gel, < 0.1 % crystalline silica) and SG-67 (containing 95.3 % of silica gel and 4.7% ammonium fluorosilicates) [see section 2.4.1.1 for read-across justification].

With regards to the acute oral toxicity, Dryacide powder administered at 2500 mg/kg bw to rats induced 2/10 mortalities. Even if this study was not performed with the applicant's silica, the results provide a good estimation of the acute oral toxicity of the active substance (LD50 > 2 000 mg/kg bw). Furthermore silicon dioxide is approved as a food additive; therefore, no further study has been required.

With regards to the acute dermal toxicity, a LD50 > 3160 mg/kg bw was obtained with SG-67. Even if the read-across is not accepted by the RMS, a low acute dermal toxicity is expected for the notified silicon dioxide Kieselguhr considering the insolubility of the substance in water and the absence of irritant potential.

With regards to the acute inhalation toxicity, exposure to Dryacide powder did not induce any mortality at 25000 mg/m^3.

Irritation – Sensitisation

No study was performed with the notified silicon dioxide Kieselguhr. Studies were submitted with Dryacide powder (containing > 90 % silicon dioxide Kieselguhr, < 10 % silica gel, < 0.1 % crystalline silica) [see section 2.4.1.1 for read-across justification].

- **Irritation**

After application of Dryacide powder under occlusion for 24 hours on the skin (intact or abraded) of 6 rabbits, no erythema or oedema was observed at 24 and 72 hours after the exposure.

Application of Dryacide powder to rabbit's eye led to a very mild irritation reversible in 3 days.
No specific data are available concerning the respiratory tract irritation potential of natural silicon dioxide. However, the repeated dose toxicity study by inhalation showed that the notified substance induced inflammatory reactions as characterized by changes in neutrophil and macrophage counts in the bronchoalveolar lavage fluid and an increase of alveolar macrophages in the lungs.
In conclusion, no additional data has been required and no classification is required for these endpoints.

- **Sensitization**

No skin sensitization is available with the notified silica. However, no particular concern has been identified in spite of the ubiquitous nature of silicon dioxide. Furthermore, given the inherent physico-properties of silicon dioxide Kieselguhr, there is no structural alert which indicates any potential for sensitization. No information on respiratory sensitization is available.
In conclusion, no additional data has been required and no classification is required for these endpoints.

In the scientific literature, a relationship between exposure to various forms of silica dust (including SAS nanoparticules or sand) and aggravation of allergic airway disease (asthma) has been observed in animals and humans.

In Brandenberger et al., 2013, the potential of polyethylene glycol coated amorphous silica nanoparticles (SNP, 90 µm diameter) to promote allergic airway disease has been investigated. Mice were sensitized by intranasal instillation with ovalbumin (OVA; allergen) and co-exposed to SNP. Upon OVA challenge, a dose-dependent enhancement of allergic airway disease is observed leading to the conclusion that allergic sensitization could be enhanced by airway exposure to engineered SNP. SNP may act as inhaled adjuvants to enhance the development and the severity of allergic airway disease in mice.

According to Park et al., 2015, acute exposure to SNP induced significant airway inflammation and airway hyper-responsiveness. Mice sensitized with OVA showed significant airway inflammation after acute exposure to SNP.

In Watanabe et al., 2015, the relationship between sand dust particles and pulmonary function, and respiratory symptoms have been investigated in adult patients with asthma. Sand dust particles were significantly associated with worsened lower respiratory tract symptoms in observed patients, but no with pulmonary function.

Many granular dust particles presented the same effects; these are not specific to natural silica or SAS.

Repeated dose toxicity

- **Repeated-dose toxicity studies by oral route:**

No repeated-dose toxicity studies by oral route are available with the notified silica. Read-across from a study with silicon dioxide Kieselguhr was accepted since the tested material contains a higher content of natural silica than that is specified for the notified silicon dioxide Kieselguhr.

Silicon dioxide Kieselguhr was administered to rats at 1, 3 or 5 % in the diet for 90 days. According to the default values in the TGD on Risk Assessment, the dosages correspond to about 820 mg/kg bw/day, 2470 mg/kg bw/day and 4120 mg/kg bw/day. After the first week, body weight gain higher than controls was observed in the 5% group (maximum during the sixth week). Estimations showed that the 3% group presented a similar weight gain than animal at the highest dose while the 1% group had weight gains similar to those of controls. No increase of silica content was observed in the liver, kidneys and spleen. No change in organ weight (liver and kidneys) was observed, except a slightly decrease in the relative spleen weight in the 5% female group but was not associated with any histopathological effects. The results lead to a NOAEL > 5%.

In conclusion, the study carried out at high doses (higher than those recommended in the OECD guidelines) does not show systemic effect, demonstrating the very low toxicity and/or low oral absorption of silicon dioxide Kieselguhr.

- **Repeated-dose toxicity studies by dermal route:**

A justification for non-submission of data was accepted for repeated-dose toxicity by dermal route. Considering the absence of irritation potential, the lack of systemic effect in a 90-day oral study (see above) and because of the low potential of dermal penetration, it is considered that no hazards are expected after repeated dermal administrations.
However, due to the mode of action of the active substance, a labelling EUH 066: Repeated exposure may cause skin dryness or cracking, is proposed.

- **Repeated-dose toxicity studies by inhalation:**

In the initial dossier, no study was submitted for the notified silica and the registrant proposed a read-across from synthetic amorphous silica to fulfil this endpoint. Since the RMS is of the opinion that no read across based on physico-chemical data can be established between synthetic and natural silica for this endpoint (see section 2.4.1.1), a 90-day inhalation study performed with the notified silica was required. In response, the applicant submitted the following 28-day inhalation study.

Sprague Dawley rats were exposed nose-only to an aerosol dust of the notified silicon dioxide Kieselguhr at target concentrations of 0.5, 1 and 5 mg/m³ (corresponding to actual concentrations of 0.58, 1.13 and 5.2 mg/m³) for 6 h/day on 5 days/week for 4 weeks. Increased respiration rate was observed following exposure during the first week of exposures in the 1 and 5 mg/m³ males and females, but did not persist in the remaining weeks. Microscopic analysis of the bronchoalveolar lavage samples showed higher mean percentage neutrophil and lower mean percentage macrophage values in the 5 mg/m³ group males and females at day 26 and 27, respectively. A partial recovery was observed at the end of the recovery period with only non-statistically significant higher mean percentage neutrophil values in females at the highest concentration. Fragments of silicon dioxide Kieselguhr were noted in all treated groups with partial to full recovery during the recovery period. Multinucleated cells, macrophages containing phagocytized cellular debris and/or blue to green cytoplasmic pigment, most likely resultant of breakdown of hemoglobin were occasionally noted in all the test substance-treated groups at all endpoints evaluated. These changes were considered to be test substance-related; although a dose-response pattern was not evident. Statistically significant higher mean lung weight relative to final body weight was observed in the highest dose group males and females at the end of the exposure period and correlated with the minimally increase of alveolar macrophages.

At microscopic examination, lungs XXXX at 5 mg/m³ exhibited minimally increased alveolar macrophages which were distributed throughout the lungs at the end of exposure period but formed multifocal aggregates in some animals at the end of recovery period. Foreign material, presumably the test substance, was identified within the cytoplasm of alveolar macrophages, although the cells were histologically unremarkable. This observation persisted at the recovery necropsy in all animals affected at 5 mg/m³ but without progression of the lesion.

In conclusion, lung inflammation as evidence by increased relative lung weight associated with accumulation of alveolar macrophages and changes in macrophage and neutrophil counts in the bronchoalveolar lavage fluid was found at the highest concentration of 5 mg/m³. Accumulation of macrophages with foreign material persisted at this concentration after a 4-week recovery period. In this context, a NOAEC of 1 mg/m³ was set.

Although effects may not have been very severe at 28 days, progression into fibrosis (in particular as the result of neutrophil infiltration) with lung function changes may be expected as for similar materials (synthetic amorphous silica). A classification STOT RE 2 – H373: May cause damage to lungs through prolonged or repeated exposure via inhalation, is proposed.

Genotoxicity

No *in vitro* genotoxicity assay was performed with the notified silica. The following studies were submitted: Ames test with a synthetic amorphous silica (Silcron G910), an alkaline single cell gel/comet assay with an amorphous silica (Spherisorb), a study assessing induction of micro- and polynuclei by silicon dioxide Kieselguhr in mammalian cells and a study assessing the morphological transforming effects of different types of silicon dioxide Kieselguhr in mammalian cells.

None of the studies submitted has been judged as sufficiently reliable to conclude on this endpoint since they were not performed with natural diatomaceous silica and/or present several protocol limitations (no sufficient characterisation of the tested material, studies not following harmonized guidelines, relevance of the cell system questionable, treatment duration too long, dose too high …).
Moreover, the Ames test would be considered inappropriate for particulate properties of the test material. Indeed, a sufficient uptake into the cell is not sure to be achieved.

In the initial dossier, no *in vivo* genotoxicity study performed with the notified silica was submitted. A 13 week HPRT study with a synthetic amorphous silica (Aerosil 200) was submitted. Since the RMS is of the opinion that no read-across based on physico-chemical data can be established between synthetic and natural silica for this endpoint (see section 2.4.1.1) and based on the low quality *in vitro* dataset, an *in vivo* Comet assay performed with the notified silica was required and provided by the registrant.

The notified silicon dioxide Kieselguhr was tested in an *in vivo* Comet assay (OECD guideline 489) in male Wistar Han rats according to standard protocol and modified version using endonuclease treatment (human 8-oxoguanine DNA glycosylase 1; hOGG1) to detect potential induction of oxidative DNA damage. Animals were dosed intratracheally once at 1.3, 4 and 12 mg/kg bw.

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Negative group (vehicle PBS) and positive control group (ethylmethanesulfonate) were included. Two sampling times were performed (2-6 hours and 25-26 hours) after the single treatment. Both the lung and the stomach were investigated as target organs for genotoxicity.

No statistically significant increase in the mean Tail Intensity (%) was observed in lung cells at any sampling time point, either treated or not treated with hOGG1. The means tail intensity in lung cells for vehicle and positive control groups were as expected. For stomach cells, the % tail DNA values obtained for negative control slides are considered too high to ensure a sufficient sensitivity of the test system to detect a weak to moderate positive effect. Therefore, even no effects were obtained on stomach cells, these results cannot be validated.

In conclusion, clear negative results were obtained on lung using both the standard and the modified protocols. The negative results on stomach (as a possible secondary organ) cannot be validated due to inadequate control values. However, considering the lack of effect observed on the lung as a primary target organ, it is considered that genotoxicity would not occur on a secondary organ exposed in a less concentrated manner. Therefore, silicon dioxide Kieselguhr is considered having no *in vivo* genotoxicity activity.

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Carcinogenicity
No carcinogenicity study was performed with the notified silica. Justification for non-submission for a chronic assay by the oral route has been accepted since amorphous silicon dioxide is a worldwide approved food additive (EPA, FDA…) and because no systemic effects were reported after oral administration.

Data from IARC monograph volume 68 on silica also support the lack of carcinogenic potential of silicon dioxide Kieselguhr. Sprague-Dawley rats received each day 20 mg/animal silicon dioxide Kieselguhr (particle size unspecified) mixed with cottage cheese at a concentration of 5 mg/g cheese in addition to commercial rat chow and filtered tap-water ad libitum. The animals were observed for life span (mean survival, 840 days after the start of treatment). IARC concludes there is inadequate evidence in experimental animals for the carcinogenicity of uncalcined silicon dioxide Kieselguhr.
The concern with silicon dioxide is rather a potential local carcinogenicity in lungs by inhalation, however, no carcinogenicity study by inhalation was available for the notified silica.
In the 28-d study in rats exposed via inhalation route, minimally increased alveolar macrophages were shown to be fully reversible at 1 mg/m^3, but were also seen in recovery group animals at the highest exposure level (5 mg/m^3). However, there was no progression/deterioration of these effects during the recovery period and therefore no indication of an ongoing inflammatory process or an increase in inflammatory parameters. Nevertheless, more severe effects could be expected following a longer exposure period.

Studies with silica-exposed workers were provided for this endpoint but none were performed with a silica comparable to the one notified in this dossier. The IARC monograph volume 68 on silica concludes there is inadequate evidence in humans for the carcinogenicity of amorphous silica.

Toxicity on the reproduction and teratogenicity

- **Developmental toxicity**

No study is available with the notified silica. Read-across from a synthetic amorphous hydrophilic silica aerogel (Syloid) was submitted by the applicant. RMS considered that data from synthetic silica can be used as supportive information for this endpoint based on the low expected oral absorption, the insolubility in water, the absence of irritation/sensitization potential and the lack of systemic effect in repeated dose toxicity studies for natural and synthetic amorphous silica.

Rats, mice, hamsters and rabbits were exposed during the organogenesis period to Syloid up to 1340 mg/kg bw/day, 1350 mg/kg bw/day, or 1600 mg/kg bw/day, depending on the species tested. No teratogenic effects were observed up to the highest dose tested.

- **Fertility**

No fertility study was performed with the notified silica. Only a 1-generation study performed with a hydrophobic silica was submitted. RMS is of the opinion that no read across based on physico-chemical data can be established between silicon dioxide Kieselguhr and synthetic amorphous silica. Furthermore, this silica has a surface treatment which can have an impact on physico-chemical properties (solubility, log Pow, shape (CH3 connection)…). Finally, the applicant does not submit a scientific justification concerning the relevance of this read-across.
However, the data gap is accepted given the low oral absorption expected, the absence of systemic effects observed in the experimental studies and the ubiquitous nature of silicon dioxide Kieselguhr.

The substance is not classified for the teratogenicity and toxicity on the reproduction.

Neurotoxicity

There is no data available which indicates that silicon dioxide may have neurotoxic properties. Considering the lack of systemic toxicity and the absence of structural alerts for neurotoxicity, generation of test data to determine neurotoxic effects of silicon dioxide is therefore not considered scientifically necessary.

AEL and MOE approach/determination

- **Choice of the critical values:**

Since no systemic effects were observed in the studies by oral and inhalation routes, no AELs have been derived. The risk assessment will only be focused on local effects. This approach had already been accepted during European technical meetings for the biocidal substances, amorphous synthetic silica gel and amorphous synthetic treated-surface silica.

Acute, medium and long-term AECs were derived for inhalation and were based on the 28-day inhalation study performed with the notified silicon dioxide Kieselguhr. In this study a NOAEC was set at 1 mg/m^3 based on the changes in the bronchoalveolar fluid (macrophage and neutrophil counts), increased relative lung weight associated with minimally increased alveolar macrophages.

- **Choice of the safety factors:**

An intra-species assessment default factor of 10 is adopted since it is considered that information on intra-species variation for local effects is very scarce; thus it is generally suggested not to refine this factor.

As far as only local effects are observed, a refined inter-species factor is proposed. It is assumed that toxicokinetics does not contribute significantly to inter-species differences. In this context, the applied factor for inter-species variations is set at 2.5 to take into account toxicodynamic differences.

A factor of 3 is used to extrapolate the duration of exposure from sub-acute to subchronic. A further factor of 2 was considered to derive the chronic AEC.

- **Derivation of the AEC:**

Since the observed local effects are due to the accumulation of silicon dioxide Kieselguhr in animal lungs, the deposited dose is correlated to the exposure duration. A longer exposure within the day will therefore lead to higher accumulation of silicon dioxide Kieselguhr. Furthermore, since all workers exposure estimations were expressed as an 8h TWA (time weight average) and as the exposure duration of tested animals in the 28-day inhalation study was 6 hours, the AEC values are corrected for an 8h exposure duration by a correction factor. Therefore AEC are expressed as 8h TWA.

The acute AEC is the NOAEC (1 mg/m3) from the 28-day inhalation study divided by an overall assessment factor of 25 (2.5 for inter-species variation and 10 for intra-species variation). Taking into account the daily exposure time of the 28-day study of 6h per day, a short-term AEC 8h TWA of 0.030 mg/m3/d is derived.

$AEC_{short\text{-}term}$ = 1 mg/m3 / AF 25 x 6h/8h/d = 0.04 mg/m3 x 6h/8h/d = 0.030 mg/m^3/d (8h TWA)

The medium-term AEC is the NOAEC (1 mg/m3) from the 28-day inhalation study divided by an overall assessment factor of 75 (2.5 for inter-species variation, 10 for intra-species variation and 3 for duration extrapolation from sub-acute to sub-chronic). Taking into account the daily exposure time of the 28-day study of 6h per day, a medium-term AEC 8h TWA of 0.010 mg/m^3/d is derived.

$AEC_{medium\text{-}term}$ = 1 mg/m3 / AF 75 x 6h/8h/d = 0.013 mg/m3 x 6h/8h/d = 0.010 mg/m^3 /d (8h TWA)

The long-term AEC is the NOAEC (1 mg/m3) from the 28-day inhalation study divided by an overall assessment factor of 75 (2.5 for inter-species variation, 10 for intra-species variation and 6 for duration extrapolation from sub-acute to chronic). Taking into account the daily exposure time of the 28-day study of 6h per day, a long-term AEC 8h TWA of 0.0050 mg/m3/d is derived.

$AEC_{long\text{-}term}$ = 1 mg/m^3 / AF 150 x 6h/8h/d = 0.007 mg/m^3 x 6h/8h/d = 0.0050 mg/m^3 /d (8h TWA)

A default dosimetric adjustment factor of 1 between rats and human has been applied. The use of an adjustment factor is not recommended in the BPR guidance Volume III Human Health – Part B Risk Assessment, but only in the REACh regulation guidance. However, the eCA is of the opinion that such adjustment may be applied.

These retained values are considered conservative as occupational exposure limits for silicon dioxide Kieselguhr in several countries range from 1 to 3 mg/m^3 for respirable fraction and from 4 to 10 for inhalable fraction. However, it was preferred to derive the AECs from a well-conducted study rather than using current occupational exposure limits (OELs) because the existing values are different depending on countries and because no scientific basis was found behind the derivation of these OELs.

Systemic effects		
	AEL [mg/kg bw /d]	**MOE_{ref} [-]**
short-term medium term long-term	**Not relevant**	**Not relevant**
Local effects (inhalation)		
	AEC 8h TWA[mg/m³ /d]	**MOE_{ref} [-]**
Short-term	0.030	25
medium-term	0.010	75
long-term	0.0050	150

- **Occupational exposure:**

Long-term occupational exposure limits for silicon dioxide Kieselguhr exist in several countries. For respirable dust, the following limits values (8 hours) were found in the GESTIS database: 1.2 mg/m3 (aerosol) in the United-Kingdom, 1.5 mg/m^3 (aerosol) in Denmark and 3 mg/m^3 in Spain. For inhalable dust, the following limits values (8 hours) were found in the GESTIS database: 4 mg/m3 in Austria, Germany and Switzerland and 10 mg/m3 in Spain.

Effect assessment of the representative product:

The representative product is 100% of the active substance, i.e. 100% of silicon dioxide Kieselguhr. In consequence, no data on the product was submitted.

2.2.1.2. Exposure assessment

The representative product INSECTOSEC containing 100 % of the active substance is dustable powder which is applied as dry dust with a handheld blow and vacuum gun, dust barrier and as surface treatment.

The exposure of the following users is assessed:

- professional dusting at a large scale in storage facilities: the product is dispensed on a large scale at up to 10 g/m^2 using hand-operated or electrostatic dusters – (chronic exposure is considered)
- professional dusting at a large scale in stables: the product is applied on a large scale at 50 g/m2 using hand-operated or electrostatic dusters. Application directions are overhead, level or downwards – (chronic exposure is considered)
- non-professional dusting for crack and crevice treatment: for amateur use, small dusting bellows are used at 10 g/m^2. – (acute exposure is considered)
- non-professional pouring of dust barriers: to prevent infestation of residential areas, InsectoSec can be poured onto the floor to create a dust barrier against crawling arthropods. This is achieved via a pouring bottle with an application rate of 5 g/m. – (acute exposure is considered)

Exposure path	Industrial use	Professional use	General public	Via the environment
Inhalation	*No*	*Yes*	*Yes*	*No*
Dermal	*No*	*Yes*	*Yes*	*No*
Oral	*No*	*No*	*No*	*No*

2.2.1.2.1. *Direct Exposure*

2.2.1.2.1.1. *Professional - Direct Exposure*

Table 2.2.1-1: Large-scale dusting in food processing and storage facilities - Combined exposure

	Mixing and loading (mg a.s./m^3 8h TWA)	**Application** (mg a.s./m^3 8h TWA)	**Total exposure** (mg a.s./m^3 8h TWA)
Tier 1 (No RPE)	6.55 x 10^{-1}	22.75	23.41
Tier 2 (RPE APF 40)	1.64 x 10^{-2}	5.69 x 10^{-1}	5.85 x 10^{-1}

Table 2.2.1-2: *Large-scale dusting in poultry pens - Combined exposure*

	Mixing and loading (mg a.s./m^3 8h TWA)	**Application** (mg a.s./m^3 8h TWA)	**Total exposure** (mg a.s./m^3 8h TWA)
Tier 1 (No RPE)	3.28	22.75	26.03
Tier 2 (RPE APF 40)	8.19 x 10^{-2}	5.69 x 10^{-1}	6.51 x 10^{-1}

2.2.1.2.1.2. *Non-professional - Direct Exposure*

Table 2.2.1-3: Dusting for crack and crevice treatment using a handheld bellow

	Application (mg a.s./m^3 8h TWA)
Tier 1 (No RPE)	0.784

Table 2.2.1-4: *Application of dust barriers using a pouring bottle*

	Application (mg a.s./m^3 8h TWA)
Tier 1 (No RPE)	0.026

2.2.1.2.2. *Indirect Exposure as a result of use of the active substance in biocidal product*

- *Professional indirect exposure:*

As professional uses lead to unacceptable risk, no secondary exposure assessment after professional applications has been performed.

- *Non-professional indirect exposure:*

1) Indirect exposure following crack and crevice treatment

As non-professional use in crack and crevice with a handheld bellow leads to unacceptable risks no secondary exposure assessment has been done.

2) Indirect exposure following dust barrier treatment

The barrier will stay in place several weeks. Silicon dioxide Kieselguhr will not spontaneously become airborne. Indeed, there is a need of an event that will force the particles to become airborne. As the barrier needs to stay intact to be efficacious, it will not be placed where people can easily walk on etc … Thus, such an event is considered rare and exposure to dust by inhalation will be considered as an acute exposure.

The product which is spilt during application or old silicon dioxide Kieselguhr powder will be removed by wiping or mopping of treated surfaces with water. Although some of the dust will be dispersed, the greatest part is inactivated as soon as it comes into contact with water or wet cleaning tools. However, the resulting air concentrations will be much lower than the concentrations during the treatment procedure. Thus, a safe use by non-professional users implies safety for cleaning activities.

Removal of dust on the floor must be done by wet cleaning. Wet cleaning will render the dust clumpy and non-dusty. Therefore, secondary exposure of adults to silicon dioxide Kieselguhr during cleaning procedures is negligible compared to exposure during the non-professional use.

Consequently, the risk assessment will be based on exposure assessment of non-professionals during application.

3) Indirect exposure via food

The substance under consideration and relevant for the claimed application is a natural silicon dioxide, also named "silicon dioxide Kieselguhr" or "silice kieselguhr" (CAS N° 61790-53-2).

InsectoSec consists of a dry silicon dioxide Kieselguhr powder produced to protect poultry pens (application rate: 50 g/m^2), private households, processing industry facilities, bakeries, glasshouses (application rate: 10 g/m^2) (with an objective of general disinsectisation). Considering intended uses, secondary exposure to professional and general public via food and/or feed is possible.

Silicon dioxide is internationally listed as food additive E 551, natural silicon dioxide as E 551c. Indeed, silicon dioxide (E551) is used as an anti-caking agent only in foods in dried form (i.e foods dried during the production process, and mixtures thereof) with maximum level of 10 g/kg[5]. Silicon dioxide is also an additive authorized in feed[6]. Kieselguhr considered in the framework of this evaluation is rather similar but is not fully compliant with the specification of food grade silicon dioxide (E 551) as required in the food additives regulation (regulation (EC) No 231/2012[7]). After experimental determination, the content of arsenic in intended kieselguhr is higher (5.4 mg/kg) than the accepted

[5] Annex II – Commission regulation (EU) No 1129/2011 of 11 November 2011 amending Annex II to regulation (EC) No 1333/2008 of the european Parliament and of the council by establishing a Union list of food additives (OJ L 295, 12.11.2011)
[6] Community Register of Feed Additives pursuant to Regulation (EC) No 1831/2003, Appendixes 3&4, Annex: List of additives, Released 21 October 2008 [Rev. 35]).
[7] Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food addtives listed in Annex II and III to Regulation (EC) No 1333/2008 of the european Parliament and of the council (OJ L 83, 22.3.2012)

level of 3 mg/kg of arsenic in the food grade forms of silicon dioxide (E 551). This higher level of arsenic in silice kieselguhr will not cause health risk for consumer.

As a plant protection product, kieselguhr (CAS N° 61790-53-2) is also used as insecticide. It is registered for the direct application in stored grain and for treatment of buildings (empty buildings, rooms, mills and stores) with no adverse effects on human health with respectively proposed maximum application rate of 2 g/kg in stored grain and 10 g/m2 for building treatment[8,9]. In "Conclusion on the peer review of the pesticide risk assessment of the active substance kieselguhr (silicon dioxide Kieselguhr)"[8], EFSA concluded that a consumer risk assessment was not required. Moreover, kieselguhr is temporarily included in Annex IV of commission Regulation (EC) No 396/2005[10] which includes active substances for which it is not necessary to set maximum residue levels.

The US Food and Drug Administration (FDA) has classified silicon dioxide as "Generally Recognised as Safe" (GRAS) and has approved its use as a dietary food additive at levels of up to 2% by weight in food. In agreement with the review by the US Environmental Protection Agency (EPA), the FDA considered that exposure to amorphous silicon dioxide in food does not pose any risk for Humans.

Considering intended uses, consumer exposure to kieselguhr residues via food or feed items will be much lower compared to consumer exposure to kieselguhr occurring as natural food ingredient.
Moreover, Kieselguhr intestinal absorption is considered limited based on physico-chemical (insolubility in water) and toxicological properties (no irritant and sensitizing properties which can improve absorption). Therefore, intake via ingestion of kieselguhr is negligible for livestock and consumers.

Besides, the Acceptable Daily Intakes (ADI) for silicon dioxide and certain silicates was qualified as "not specified" by the JECFA during its 29th meeting (1985).
According to available toxicological data, no systemic effects after ingestion of kieselguhr are expected. Therefore, no acceptable daily intake (ADI) and no acute reference dose (ARfD) have been set for kieselguhr (see doc IIA).

As a conclusion, considering available knowledge about the nature of kieselguhr, its physico-chemical properties, toxicological effects and regulations already in force, indirect exposure to kieselguhr via food/feed for intended biocide uses in PT18 will be negligible.

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[8] European Food Safety Authority (EFSA): Conclusion on the peer review of the pesticide risk assessment of the active substance kieselguhr (diatomaceous earth), EFSA Journal 2012;10(7):2797

[9] FINAL Review Report for the active substance kieselguhr (diatomaceous earth) finalised in the standing committee on the Food chain and Animal Health at ist meeting on 28 ctober 2008 in view of the inclusions of kieselguhr (diatomaceous earth) in Annex I of directive 91/414/EEC (Document SANCO/2617/08-rev.5))

[10] Commission Regulation (EC) No 839/2008 of 31 July 2008 amending Regulation (EC) No 396/2005 of the european Parliament and oft he council as regards Annexes II, III and IV on maximum residue levels of pesticides in or on certain products.

2.2.1.2.3. *Summary of human exposure*

Tier	**Time frame**	**Inhalation exposure**		**Dermal exposure** [b]		**Oral exposure** +	**Total exposure** +
PPE	Frequency	8h TWA Actual air concentration	Systemic dose[a]	Deposit on skin	Systemic dose[a]	Systemic dose[a]	Systemic dose[a]
		mg as /m³ air	mg as / kg bw /day	mg as /day	mg as / kg bw /day	mg as / kg bw /day	mg as / kg bw /day
Task:		**Professional application during dusting in food processing and storage facilities**					
Tier 1: **Without PPE**	Mixing and loading application	**23.41**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Tier 2: (**RPE APF 40)**		**5.85 x 10⁻¹**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Task:		**Professional during *large scale dusting in stables***					
Tier 1: **Without PPE**	Mixing and loading application Application	**26.03**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Tier 2: (**RPE APF 40)**		**6.51 x 10-1**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Task:		**Non-Professional *during crack and crevice treatment***					
Tier 1: **Without PPE**	Application	**0. 784**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Task:		**Non-Professional *during during pouring of dust barrier***					
Tier 1: **Without PPE**	Application	**0.026**	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*

2.2.1.3. Risk characterisation

2.2.1.3.1.1. *Direct Exposure*

- **Professional users**

Risks for professional exposed during dusting in food processing and storage facilities

Exposure Scenario	**Inhalation exposure** (mg a.s./m^3 8h TWA)	**NOAEC** (mg/m^3)	**AF MOE_{ref}**	**AEC** (mg/m^3 8h TWA)	**MOE**	**Exposure (%AEC)**
Tier 1 (no RPE)	23.41	1	150	0.005	0.04 3	468104
Tier 2 (RPE APF 40)	5.85×10^{-1}	1	150	0.005	1.71	11703

The exposure of professionals to silicon dioxide Kieselguhr during the dusting in food processing and storage facilities leads to an unacceptable risk.

Risks for professional exposed large scale dusting in stables

Exposure Scenario	**Inhalation exposure** (mg a.s./m^3 8h TWA)	**NOAEC** (mg/m^3)	**AF MOE_{ref}**	**AEC** (mg/m^3 8h TWA)	**MOE**	**Exposure (%AEC)**
Tier 1 (no RPE)	26.03	1	150	0.005	0.04	520520
Tier 2 (RPE APF 40)	6.51×10^{-1}	1	150	0.005	1.54	130130

The exposure of professionals to silicon dioxide Kieselguhr during the large scale dusting in stables leads to an unacceptable risk.

- **Non-professional users**

Risks for non - professional exposed during crack and crevice treatment using a hand held bellow

Exposure Scenario	Inhalation exposure (mg a.s./m³ 8h TWA)	NOAEC (mg/m³)	AF MOE_{ref}	AEC (mg/m³)	MOE	Exposure (%AEC)
Tier 1 (no RPE)	0.784	1	25	0.03	**1.28**	**2613**

The exposure of non-professionals to silicon dioxide Kieselguhr during the dusting in crack and crevice leads to an unacceptable risk.

Risks for non - professional exposed during pouring of dust barrier

Exposure Scenario	Inhalation exposure (mg a.s./m³ 8h TWA)	NOAEC (mg/m³)	AF MOE_{ref}	AEC (mg/m³ 8h TWA)	MOE	Exposure (%AEC)
Tier 1 (no RPE)	0.026	1	25	0.03	38.4	87

The exposure of non-professionals to silicon dioxide Kieselguhr during the pouring phase as a dust barrier leads to an acceptable risk.

2.2.1.3.1.2. *Indirect Exposure as a result of use*

- **Professional indirect exposure**

As professional uses do not lead to acceptable risks no secondary exposure assessment has been done for secondary exposure after professional application.

- **General public indirect exposure**

Risks for indirect exposure following crack and crevice treatment
As non-professional use in crack and crevice with a handheld bellow does not lead to acceptable risks, no secondary exposure assessment has been done.

Risks for indirect exposure following dust barrier treatment
Concerning application of dust barrier, as concluded in the exposure assessment, indirect exposure as result of non-professional use will be lower than during application so the result of the risk assessment of the application will cover the risk of indirect exposure.

As a result, indirect exposure to silicon dioxide Kieselguhr following dust barrier treatment leads to an acceptable risk.

- **Indirect exposure via food**

Considering available knowledge about the nature of Kieselguhr, its physico-chemical properties, toxicological effects and regulations already in force, indirect exposure to Kieselguhr via food/feed for intended biocide uses in PT18 will be negligible and is considered of low relevance.

2.2.2. Environmental Risk Assessment

Silicon dioxide occurs ubiquitously in the environment. It accounts for approximately 27.6% of the earth's crust and is widely distributed in water, soils and plant and animal tissues. Silicon dioxide is regarded as inert in all but extreme conditions.

Silicon dioxide Kieselguhr is almost amorphous silicon dioxide made up of fossilised diatoms. Silicon dioxide Kieselguhr is a geological deposit consisting of the fossilised skeletons of numerous species of siliceous marine and freshwater one-cellular organisms, particularly diatoms and other algae (Korunic, 1998). Many of these fossilised sedimentary layers originated at least 20 million years ago in the lakes and seas of the Eocene and Miocene Epochs.

2.2.2.1. Fate and distribution in the environment

Degradation
Silicon dioxide Kieselguhr is an inorganic molecule and not soluble in water. There is no abiotic, biotic or chemical degradation of the fossilized diatom algae. Silicon dioxide is stable and does not form metabolites or degradation products.

Biodegradation
Biodegradation study is not applicable, as silicon dioxide Kieselguhr is an inorganic compound. Earth is mainly formed of polymerically bound silicon dioxide (SiO_2) which is very stable and insoluble in water and not accessible to biological transformation.

Abiotic degradation
Silicon dioxide Kieselguhr as fossilized diatom algae is an inorganic molecule and not soluble in water. It is not susceptible to aqueous photochemical or hydrolytical degradation mechanisms. The vapour pressure is negligible at ambient temperatures. Therefore volatilisation into the air and photodegradation in this compartment is not relevant.

Distribution
Silicon dioxide Kieselguhr is a natural raw material which mainly contains silica (60-97% SiO_2). Silicon is the second most abundant chemical element, after oxygen, in the earth's crust accounting for 28.15% of its mass. Silicate minerals (such as plagioclase, alkali feldspars, pyroxenes, amphiboles, micas and clays, excluding silica) comprise together 80% by volume of the earth's crust. Soils contain up to 95% SiO_2. Al_2O_3, Fe_2O_3 and clay minerals are most common in soils. Silicon dioxide Kieselguhr itself as well as all its components naturally occurs in almost all kind of soils.

Silicon dioxide Kieselguhr itself may even be a natural component of some soils or rather build up own soil horizons. Considering the physicochemical properties of silicon dioxide Kieselguhr (non-soluble, high density, and negligible vapour pressure), silicon dioxide

Kieselguhr released into the environment is expected to be distributed mainly into the soil and sediment compartment and probably not at all into water or air, unless in particular form. Amorphous silica, main component of silicon dioxide Kieselguhr, is expected to combine indistinguishably with the soil or sediment due to their similarity with inorganic soil/sediment matter.

Bioaccumulation
Silicon dioxide Kieselguhr is chemically inert. It is not soluble – neither in water, nor in lipids and has no lipophilic properties. In consequence, it is neither feasible to determine a BCF. Diatomaceous Earth has not at all intrinsic potential for bioconcentration.

In conclusion, bioconcentration of silicon dioxide Kieselguhr is considered to be not an issue of concern due to its physico-chemical properties.

2.2.2.1. Hazard identification and effects assessment

Aquatic compartment (including water, sediment and STP)
Silicon dioxide Kieselguhr is fossilized diatom algae. Diatoms are unicellular autotrophic algae which live in all kinds of marine and freshwater environments. Thus, diatoms are a natural compound of all aquatic ecosystems as primary producers in the photic zone. Silicon dioxide Kieselguhr is a natural component of all aquatic ecosystems and is chemically inert and non-soluble, neither in water, nor in lipids. Due to its insolubility and density, silicon dioxide Kieselguhr will undergo sedimentation if it enters natural water bodies. Considering its origin and composition, silicon dioxide Kieselguhr is impossible to differentiate from the naturally occurring silicates in the sediment.

In water and under high relative humidity silicon dioxide Kieselguhr becomes water saturated and looses its insecticidal effect. For the sake of completeness acute ecotoxicity tests with fish, daphnids and algae have been conducted as limit test with a concentration of 100 mg/L test item. A test regarding the respiration inhibition of activated sludge has been performed with concentrations up to 1000 mg/L.

Concerning the expression of the endpoints, normally the rule is to set the LC50 to the solubility limit. However, the substance being insoluble and without effect on aquatic organisms at high concentrations, endpoints values based on solubility limit would not reflect any kind of reality at all. It seems therefore more consistent to define the endpoint values from nominal concentrations.

Moreover, in the case of amorphous hydrophobic silicon dioxide, it has been considered that long term studies are not required because there is no long term exposure (agreement reached during TMIII10). Indeed, even if the substance does not degrade, the substance is not soluble in water; therefore the substance is not bioavailable for aquatic organisms. Applying the same approach for silicon dioxide Kieselguhr is considered acceptable by the RMS.

Moreover:
- Due to the indirect emission only in surface water or soil and,
- Due to the physico-chemical properties of the substance, which leave the substance in the solid phase, the exposure of the surface water would be unlikely.
- In STP compartment, the substance will be totally removed with all other solid phase in sludge.

Therefore no emission to surface water is expected. Then, after sludge released on soil, substance will stay in the soil layer.

PNEC for aquatic organisms

Acute ecotoxicity tests with fish, daphnids and algae have been conducted as limit test with a concentration of 100 mg/L test item.

Guideline / test method	Test species	Endpoint/ type of test	Exposure design/ duration	Result based on nominal concentration [mg a.s. L^{-1}]		
				LC_0	LC_{50}	LC_{100}
92/69/EEC, C.1, 1992 OECD No. 203, 1992	Fish (*Oncorhynchus mykiss*)	LC_{50}, limit test	Static 96 h	≥ 100	> 100	> 100
92/69/EEC, C.2, 1992 OECD No. 202, 2004	Daphnid (*Daphnia magna*)	EC_{50}, limit test	Static 48 h	≥ 100	> 100	> 100
92/69/EEC, C.3, 1992 OECD No. 201, 1992	Algae (*Desmodesmus subspicatus*)	EC_{50}, NOEC, limit test	Static 72 h	≥ 100	> 100	> 100

All the endpoints were EC50 or LC50 values > 100 mg a.s./L. According to the TGD a safety factor of 1000 should be applied to the lowest endpoint for aquatic environment when one short-term from each of three trophic levels is available.

Hence, the PNECaquatic is estimated to be 0.1 mg a.s./L (nominal concentration).

PNEC for STP micro-organisms

A test regarding the respiration inhibition of activated sludge has been performed with concentrations up to 1000 mg/L.

Guideline / test method	Test species	Endpoint/ type of test	Exposure design/duration	Result based on nominal concentration [mg a.s. L^{-1}]		
				NOEC	EC_{20}	EC_{50}
88/302/EEC, 1988 OECD No. 209, 1984	Micro organisms Activated sludge	NOEC, EC_{50}	Static 3 h	1000	> 1000	> 1000

In order to prevent adverse effects of silicon dioxide Kieselguhr on microbial activity in STPs, a PNECmicroorganisms was derived from the respiration inhibition test according to the OECD guideline 209. The NOEC obtained (1000 mg a.s./L) divided by an assessment factor of 10 would have led to a PNECmicroorganisms of 100 mg a.s./L (nominal concentration).

PNEC for sediment

In the absence of any ecotoxicological data for sediment-dwelling organisms, the PNECsediment is generally calculated with the equilibrium partitioning method. This method uses the PNECaquatic for aquatic organisms and the suspended matter/water partitioning coefficient as inputs. Equilibrium partitioning method (EPM) is based on the assumption that sediment toxicity expressed in terms of the freely-dissolved substance concentration in the pore water is the same as aquatic toxicity. The pore water concentration is correlated with the bioavailable fraction.

However, silicon dioxide Kieselguhr is an inorganic substance, insoluble in water; the Kow and Koc concept is therefore not applicable. The EPM which is based on partitioning coefficient Ksuspended-matter-water cannot be used as for organic compounds to define a PNECsediment value.

Moreover, as silicon dioxide Kieselguhr under normal conditions of use in biocidal product will be applied indoors only, the contamination of the aquatic compartment will be indirect and no data were presented on the toxicity of these compounds to sediment-dwelling organisms.

For these reasons, no PNECsediment value was proposed for silicon dioxide Kieselguhr.

Terrestrial compartment
As silicon dioxide Kieselguhr will be applied indoors only, the contamination of the terrestrial compartment will be indirect and no data were presented on the toxicity of these compounds to terrestrial organisms, according to the BPR data requirements for active substances and biocidal products. When released into the environment, these forms are expected to combine with soil organic and inorganic matter and adopt the same behavior as natural silica. Silicon dioxide Kieselguhr itself may even be a natural component of some soils or rather build up own soil horizons. Under high relative humidity silicon dioxide Kieselguhr becomes water saturated and looses its insecticidal effect. Based on the inert character and the natural occurrence in soils of silicon dioxide Kieselguhr, adverse effects on terrestrial life are considered to be no issue of concern.

Nevertheless in order to conduct a risk assessment, it was proposed to make a comparison between PECsoil values and background levels in soil of natural silica which are in the range of 706 $g/kg_{dry\ weight}$ (corresponding to 625 g/kg_{ww}). Even if this background level represents only a mean value which does not necessarily cover the different types of soil found in the environment, this value was considered as a conservative reference value in view of the high quantity of this substance in the environment.

Non compartment specific effects relevant to the food chain (secondary poisoning)
Silicon dioxide Kieselguhr is chemically inert. It is not soluble – neither in water, nor in lipids and has no lipophilic properties. Thus, due to the physico-chemical properties silicon dioxide Kieselguhr has no potential for bioaccumulation in aquatic or terrestrial organisms.

Summary of PNEC values

ENVIRONMENTAL COMPARTMENT	PNEC	Unit
$PNEC_{STP}$	100	$mg.L^{-1}$
$PNEC_{surface\ water}$	0.1	$mg.L^{-1}$
$PNEC_{sediment\ freshwater}$	Not determined	
$PNEC_{soil}$	Not determined Natural silica background level in soil: 625 $g.kg^{-1}{}_{wwt}$	

<u>Effect assessment of the representative product:</u>
No data on product is available as the product is 100 % of the active substance.

2.2.2.2. Exposure assessment

Silicon dioxide Kieselguhr is an abrasive, fine white powder made of the tiny fossilized remains of diatoms. The granules consist of razor sharp microscopic diatoms with intricate geometric forms. The product InsectoSec which is 100% of the active substance will be used to kill crawling arthropods and ectoparasites, *e.g.* mites and lice.

The environmental exposure has been evaluated depending on the intended uses of the silicon dioxide Kieselguhr, and according to the Guidance on the BPR: Volume IV Environment, Part B Risk Assessment (active substances) (GBPR) (ECHA, 2015) and the Emission Scenario Documents (ESD) for Biocidal Product Type 18 (OECD 2006[11], OECD 2008[12]). As a prerequisite for estimation the emission rates, appropriate emission scenarios are based on the general fate and distribution of the active substance.

Silicon dioxide Kieselguhr has demonstrated an efficacy for the following intended uses as insecticide:

- in poultry houses by sprinkling at an application rate of 50 g/m² against *Dermanyssus gallinae* (adults and larvae). The ESD assumes that emission of the active substance after application in animal housing occurs mainly via manure/slurry and waste water (STP). For the number of treatment per year considered for calculations, it has been assumed that one treatment program with diatomaceus earth takes place on each cycle for poultry. As a consequence, the number of applications has been set at the default value of 4 treatment cycles, in accordance with the ESD-PT18 (OECD, 2006). A worst case was applied for the calculations by considering the efficiency result against poultry red mite (*Dermanyssus gallinae*), for which 3 applications at 50 g/m² in 28 days is needed by treatment cycle, *i.e.* 150 g/m²

- in food and feed processing industry facilities (e.g. bakeries, mills, stores), private households, glasshouses etc. The environmental contamination pathway is considered to be the drain via the sewer system into the sewage treatment plant (STP), considering the following intended uses:
    - By sprinkling at an application rate of 10 g/m² of area against *Ctenocephalides felis* (adult), *Lasius niger*, *Porcellio scaber* and *Lepisma saccharina* (adult);

    - As a dust barrier at an application rate of 5 g/m. No scenario for estimating the releases of silicon dioxide Kieselguhr from this use was applied, considering this is covered by the scenario applied for sprinkling of total surface.

2.2.2.3. Risk characterisation

The risk characterisation is summarized in the following table.

[11] OECD (2006): Emission Scenario Document For Insecticides for Stables and Manure Storage Systems. OECD Environmental Health and safety Publications. Series on Emission Scenario Documents, no 14. ENV/JM/MONO(2006)4 .

[12] OECD (2008): Emission Scenario Document (ESD) for Insecticides, Acaricides and Products to control other Arthropods for household and professional uses. Environment Directorate Organisation for economic co-operation and development, Paris.

Background level of natural silica in soil [mg.kg$_{wwt}^{-1}$] : 6.25E+05						
PEC		%background level				
PT18-indoor surface treatment by dusting in food and feed industry facilities, and private households						
Release *via* waste water						
PEC_{STP} [mg.L^{-1}]	not relevant	-				
$PEC_{freshwater}$ [mg.L^{-1}]	not relevant	-				
$PEC_{sediment}$ [mg.L^{-1}]	not relevant	-				
PEC_{soil} [mg.kg^{-1}$_{wwt}$]	3.37E+03	**0.54%**				
$PEC_{groundwater}$ [µg.L^{-1}]	not relevant	-				
PT18-indoor surface treatment by dusting in poultry houses						
Release *via* waste water						
PEC_{STP} [mg.L^{-1}]	not relevant	-				
$PEC_{freshwater}$ [mg.L^{-1}]	not relevant	-				
$PEC_{sediment}$ [mg.L^{-1}]	not relevant	-				
PEC_{soil} [mg.kg^{-1}$_{wwt}$]	covered by PEC calculated for PT18-indoor surface treatment by dusting in food and feed industry facilities, and private households					
$PEC_{groundwater}$ [µg.L^{-1}]	not relevant	-				
Release *via* slurry/manure spreading on land						
Animal Sub-cat	**Grassland**[1]				**Arable land**	
	PIECgrs-N [mg.kg^{-1}$_{wwt}$]	%background level	**PIECgrs-N$_{worst\ case}$ [mg.kg^{-1}$_{wwt}$]**	%background level	**PIECars-N [mg.kg^{-1}$_{wwt}$]**	%background level
7 - Laying hens in battery cages - no treatment	3.30E+00	**0.00053%**	1.32E+01	**0.00211%**	1.65E+00	**0.00026%**
8 - Laying hens in battery cages with aeration- belt drying	0.00E+00	-	0.00E+00	-	0.00E+00	-
9 - Laying hens in battery cages with forced drying - (deep pit, high rise)	3.28E+00	**0.00052%**	1.31E+01	**0.00210%**	1.64E+00	**0.00026%**
10 - Laying hens in compact battery cages	3.69E+00	**0.00059%**	1.47E+01	**0.00236%**	1.84E+00	**0.00029%**
11 - Laying hens in free range with litter floor	1.34E+01	**0.00215%**	5.38E+01	**0.00860%**	6.72E+00	**0.00108%**
12 - Broilers in free range - litter floor	5.81E+00	**0.00093%**	2.32E+01	**0.00372%**	2.90E+00	**0.00046%**
13 - Laying hens in free range - grating floor	6.79E+00	**0.00109%**	2.71E+01	**0.00434%**	3.39E+00	**0.00054%**
14 - Parent broilers in free range - grating floor	3.66E+00	**0.00059%**	1.47E+01	**0.00234%**	1.83E+00	**0.00029%**
15 - Parent broilers in rearing - grating floor	7.75E+00	**0.00124%**	3.10E+01	**0.00496%**	3.87E+00	**0.00062%**
16 - Turkey in free range - litter floor	1.09E+01	**0.00175%**	4.37E+01	**0.00699%**	5.46E+00	**0.00087%**
17 - Ducks in free range - litter floor	1.17E+01	**0.00186%**	4.66E+01	**0.00746%**	5.83E+00	**0.00093%**
18 - Geese in free range - litter floor	8.22E+00	**0.00132%**	3.29E+01	**0.00526%**	4.11E+00	**0.00066%**

[1] According to the ESD-PT18 (OECD, 2006), the calculation of the PIEC for grassland considered 4 manure applications per year. Considering that no degradation of silicon dioxide Kieselguhr occurs between applications, a worst case should consider a PIECgrs-Nworst-case as 4 * PIECgrs-N.

Aquatic compartment (including sediment)

Residues of silicon dioxide Kieselguhr entering the sewer system undergo immediate settling in the primary settler of the connected STP due to the physico-chemical and biological properties of silicon dioxide Kieselguhr (particle size, chemically and biologically inert, non-volatile, insolubility). A distribution in the water phase of the STP can therefore be ruled out and subsequent dilution into a surface water body (surface water / sediment) is not considered as being relevant.

Atmospheric compartment
The exposure of the atmosphere is considered as not relevant because the active substance is non-volatile.

Terrestrial compartment (including groundwater)

- ***PT18-indoor surface treatment by sprinkling in poultry pens – Release via manure/slurry application to land***

Considering manure/slurry application to grassland and arable land, initial PEC for soil correspond to less than 0.01% of the natural silica background level in soil for all poultry housing type. As a consequence, release of silicon dioxide Kieselguhr *via* manure/slurry application to land after use of InsectoSec for surface treatment by sprinkling in poultry pens should be considered negligible.
Due to its insolubility, no significant mobility of the silicon dioxide Kieselguhr to groundwater is expected.

- ***PT18-indoor surface treatment by sprinkling in poultry pens – Release via emission to the STP***

Release to waste water is expected when silicon dioxide Kieselguhr is used as PT18-surface treatment by sprinkling in poultry houses, which induced indirect releases to soil via STP sludge spreading onto soil. Taking into account the estimated emission, the RMS considers that no PEC for soil is needed to be calculated for emission *via* waste water, as these releases are covered by those calculated for the use of silicon dioxide Kieselguhr as PT18-surface treatment by sprinkling in food and feed industry facilities, and private households.

- ***PT18-indoor surface treatment by sprinkling in food and feed industry facilities, and private households***

PEC for soil after use of InsectoSec for surface treatment by sprinkling in food and feed industry facilities, and private households was 3.37E+03 $mg.kg^{-1}$wwt, which correspond to 0.54% of the natural silica background level in soil. As a consequence, release of silicon dioxide Kieselguhr after use of InsectoSec for surface treatment by sprinkling in food and feed industry facilities, and private households should be considered negligible.

Non-compartmental specific effects relevant to the food chain (secondary poisoning)
Silicon dioxide is allowed as feed additive for any group of animals without limit. The use of silicon dioxide Kieselguhr as biocide therefore cannot have any negative effects on birds or mammals. There is no need to assess this exposure route further.

Overall conclusion for the environment

Considering that:

- Silicon dioxide occurs ubiquitously in the environment. It accounts for approximately 27.6% of the earth’s crust and is widely distributed in water, soils and plant and animal tissues. Background levels in soil of natural silica which are in the range of 706 $g/kg_{dry\ weight}$ (corresponding to 625 $g/_{kgww}$).

- The intended uses of silicon dioxide Kieselguhr proposed by the applicant are uses as insecticide:

    - in poultry houses by sprinkling at an application rate of 50 g/m² against *Dermanyssus gallinae* (adults and larvae), with emissions to the environment expected to be mainly via manure/slurry and waste water (STP).

- in food and feed processing industry facilities (*e.g.* bakeries, mills, stores), private households, glasshouses etc. by sprinkling and as a dust barrier, with emission to the environment expected to be mainly via waste water (STP).

In accordance with the realistic worst case scenarios applied for the risk assessment the use of silicon dioxide Kieselguhr as PT18-insecticide in poultry houses and in food and feed processing industry facilities, privates houses, glasshouses, etc., is therefore considered acceptable, as predicted releases to relevant environmental compartment (*i.e.* soil) should be considered as negligible compared to the background level.

2.2.2.4. PBT, POP and assessment

According to the Annex XIII of Reach regulation, PBT assessment in, substances are classified PBT or vPvB when they fulfil the criteria for all three inherent properties Persistent, Bioaccumulable, Toxic.

- **Persistence criterion (P)**

The active substance silicon dioxide Kieselguhr as inorganic substance is excluded from the P assessment taking into account the Annex XIII of Reach regulation. Therefore the criterion for persistence in soil is not relevant.

- **Bioaccumulation criterion (B)**

According to the PBT assessment in ECHA guidance R11, v.2.0 (2014), a substance is considered to fulfil the B criterion when the bioconcentration factor (BCF) exceeds a value of 2000 L/kg.
While there are no studies on its bioaccumulation, silicon dioxide Kieselguhr has no potential for bioaccumulation due to its intrinsic properties.
Silicon dioxide Kieselguhr is not selected according to the B criterion.

- **Toxicity criterion (T)**

According to the PBT assessment in ECHA guidance R11, v.2.0 (2014), the toxicity criterion is fulfilled when the chronic NOEC for aquatic organism is less than 0.01 mg/L.
Based on ecotoxicity data, no classification is proposed for the substance. T criteria is therefore not fulfilled.

- **PBT Conclusion**

Silicon dioxide Kieselguhr does not fulfill the PBT criteria.

- **POP Conclusion**

The POP criterion is not relevant as silicon dioxide Kieselguhr is an inorganic substance.

2.2.3. Assessment of endocrine disruptor properties

There are no indications in the dossier which permit to conclude on the endocrine disruption properties of silicon dioxide kieselguhr.

2.3. Overall conclusions

<table>
<tr><th rowspan="2">SCENARIO</th><th rowspan="2">Application</th><th colspan="2">Human primary exposure</th><th colspan="2">Human secondary exposure</th><th rowspan="2">STP</th><th colspan="2">Aquatic compartment</th><th rowspan="2">Terrestrial compartment</th><th rowspan="2">Groundwater</th><th rowspan="2">Air</th><th rowspan="2">Secondary poisoning</th></tr>
<tr><th>Professional</th><th>Non professional</th><th>Worker</th><th>General public</th><th>Surface water</th><th>Sediment</th></tr>
<tr><td>To control poultry red mites in poultry pens</td><td>Large scale dusting</td><td>Not acceptable</td><td>NR</td><td>Not assessed*</td><td>-</td><td>NR</td><td>NR</td><td>NR</td><td>Acceptable</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td>To control insects in food and feed processing industry facilities</td><td>Large scale dusting</td><td>Not acceptable</td><td>NR</td><td>Not assessed*</td><td>-</td><td rowspan="3">NR</td><td rowspan="3">NR</td><td rowspan="3">NR</td><td rowspan="3">Acceptable</td><td rowspan="3">NR</td><td rowspan="3">NR</td><td rowspan="3">NR</td></tr>
<tr><td rowspan="2">To control insects in private households</td><td>Crack and crevice dusting</td><td>NR</td><td>Not acceptable</td><td>NR</td><td>Not assessed*</td></tr>
<tr><td>Dust barrier</td><td>NR</td><td>Acceptable</td><td>NR</td><td>Acceptable</td></tr>
</table>

*Not assessed as primary exposure is not acceptable
NR: not relevant

The outcome of the assessment for silicon dioxide kieselguhr in product-type 18 is specified in the BPC opinion following discussions at the seventeen (17) meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.4. List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	Silicon dioxide Kieselguhr (DE)
Function (*e.g.* fungicide)	Insecticide, Acaricide
Rapporteur Member State	France

Identity

Chemical name (IUPAC)	no IUPAC name
Chemical name (CA)	Silicon dioxide Kieselguhr (DE) Synonym: Kieselguhr, Diatomite
CAS No	61790-53-2
EC No	612-383-7
Other substance No.	CIPAC: 647
Minimum purity of the active substance as manufactured (g/kg or g/l)	Silicon dioxide Kieselguhr has a specified purity of 100% w/w (1000 g/kg).
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Crystalline silica < 0.1%
Molecular formula	Silicon dioxide Kieselguhr is composed of a mixture of inorganic oxides
Molecular mass	Silicon dioxide Kieselguhr is composed of a mixture of inorganic oxides
Structural formula	Silicon dioxide Kieselguhr is composed of a mixture of inorganic oxides Particle size distribution: L50D > 7 µm Specific surface area : 30 - 45 m²/g

Physical and chemical properties

Melting point (state purity)	1710 °C (100% silicon dioxide Kieselguhr)
Boiling point (state purity)	> 2200 °C (100% silicon dioxide Kieselguhr)
Temperature of decomposition	Silicon dioxide Kieselguhr shows no discrete peaks of melting points or phase transitions in thermal analysis, neither before nor after thermal treatment. Investigation for crystalline compounds shows no new crystalline phases after thermal treatment. The tests prove the thermal stability under air and humid conditions.
Appearance (state purity)	Odourless solid. The colour varies from white grey to yellow to red. (100% silicon dioxide Kieselguhr)
Relative density (state purity)	The density of silicon dioxide Kieselguhr varies between 80-320 g/L, depending on the geographical origin (100% silicon dioxide Kieselguhr).
Surface tension	Not applicable because active substance is not soluble in water.
Vapour pressure (in Pa, state temperature)	The vapour pressure is estimated to be 0 mm Hg.
Henry's law constant (Pa m^3 mol^{-1})	The active substance is not volatile.

Solubility in water (g/l or mg/l, state temperature)	not soluble
Solubility in organic solvents (in g/l or mg/l, state temperature)	not soluble
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable because active substance does not include an organic solvent.
Partition coefficient (log P_{OW}) (state temperature)	Not applicable because active substance is not soluble in water and organic solvents.
Dissociation constant	Not applicable because active substance is not soluble in water.
Flammability	Active substance does not present flammable properties.
Explosive properties	Active substance does not present any risk for explosion.

Classification and proposed labelling

with regard to physical/chemical data	No classification / labelling is required for silicon dioxide Kieselguhr in accordance CLP
with regard to toxicological data	STOT RE 2 – H373: May cause damage to organs (lungs) through prolonged or repeated exposure EUH 066: Repeated exposure may cause skin dryness and cracking.
with regard to fate and behaviour data	No classification / labelling is required for silicon dioxide Kieselguhr in accordance CLP
with regard to ecotoxicological data	No classification / labelling is required for silicon dioxide Kieselguhr in accordance CLP

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance	inorganic oxides in active substance: ICP - OES
Impurities in technical active substance (principle of method)	crystaline silica : X-ray fluorescence spectroscopy (XRF)

Analytical methods for residues

Soil (principle of method and LOQ)	no method required
Air (principle of method and LOQ)	NIOSH method: X-ray diffraction Estimated limit of detection: 0.005 mg per sample.
Water (principle of method and LOQ)	no method required
Body fluids and tissues (principle of method and LOQ)	no method required
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	no method required
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	no method required

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Not required (local effects)
Rate and extent of dermal absorption:	not required (local effects)
Distribution:	n. a.
Potential for accumulation:	No potential for accumulation.
Rate and extent of excretion:	Not determined
Toxicologically significant metabolite	none

Acute toxicity

Rat LD_{50} oral	>2000 mg/kg
Rabbit LD_{50} dermal	> 3160 mg/kg
Rat LC_{50} inhalation	> 25,000 mg/m³
Skin irritation	No skin irritation
Eye irritation	Eye (rabbit): very mild irritant
Skin sensitization (test method used and result)	No skin sensitization

Repeated dose toxicity

Species/ target / critical effect	No repeated-dose toxicity studies by oral route are available with the notified silica. Read-across from a study with "silicon dioxide Kieselguhr" was accepted since the tested material contains a higher content of natural silica than that is specified for the notified silicon dioxide Kieselguhr. 90 day study - rat
Lowest relevant oral NOAEL / LOAEL	The study carried out at high doses (higher than those recommended in the OECD guidelines) does not show systemic effect, demonstrating the very low toxicity and/or low oral absorption of silicon dioxide Kieselguhr.
Lowest relevant dermal NOAEL / LOAEL	A justification for non-submission of data was accepted for repeated-dose toxicity by dermal route. Considering the absence of irritation potential, the lack of systemic effect in a 90-day oral study (see above) and because of the low potential of dermal penetration, it is considered that no hazards are expected after repeated dermal administrations.
Lowest relevant inhalation NOAEL / LOAEL	28-day inhalation study - rat Lung inflammation as evidence by increased relative lung weight associated with accumulation of alveolar macrophages and changes in macrophage and neutrophil counts in the bronchoalveolar lavage fluid was found at the highest concentration of 5 mg/m³. Accumulation of macrophages with foreign material persisted at this concentration after a 4-week recovery period. In this context, a NOAEC of 1 mg/m³ was set.

Genotoxicity	Silicon dioxide Kieselguhr is considered having no *in vivo* genotoxicity activity.

Carcinogenicity

Species/type of tumour	No carcinogenicity study performed with the notified silica. Justification for non-submission for

	a chronic assay by the oral route has been accepted since amorphous silicon dioxide is a worldwide approved food additive (EPA, FDA…) and because no systemic effects were reported after oral administration. No data on inhalation is available.

Reproductive toxicity

Species/ Reproduction target / critical effect	Data gap accepted given the low oral absorption expected, the absence of systemic effects observed in the experimental studies and the ubiquitous nature of silicon dioxide Kieselguhr.
Lowest relevant reproductive NOAEL / LOAEL	n.a.
Species/Developmental target / critical effect	Read-across from a synthetic amorphous hydrophilic silica aerogel (Syloid)
Lowest relevant developmental NOAEL / LOAEL	> 1000 mg/kg/day

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	No neurotoxicity
Lowest relevant developmental NOAEL / LOAEL.	n. a.

Other toxicological studies

Food and feeding stuffs	- Secondary exposure to professional and general public via food and/or feed is possible. Considering available knowledge about the nature of kieselguhr, its physico-chemical properties and toxicological data, indirect exposure to kieselguhr via food/feed for intended biocide uses in PT 18 will be negligible and is consequently considered of low relevance.

Medical data

	Several exposure studies were made for silicon dioxide Kieselguhr workers in order to find out about the evidence for carcinogenicity (Cooper 1977; please also see Hazardous Substances Data Bank 2006). The overall evaluation of the International Agency for Research on Cancer in 1997 concluded that there is inadequate evidence in humans for the carcinogenicity of amorphous silica which therefore is not classifiable as to its carcinogenicity (Group 3; IARC 1997). Due to these references and worldwide positive experiences with silicon dioxide Kieselguhr from our point of view it is not necessary to create further medical data in anonymous form and Epidemiological studies. silicon dioxide Kieselguhr is used as pesticide since the late 1950`s with no negative effects reported.

Summary

Systemic effects		
	AEL [mg/kg bw /d]	**MOE_{ref} [-]**
short-term medium term long-term	**Not relevant**	**Not relevant**
Local effects (inhalation)		
	AEC [mg/m³/d] (6h exposure)	**MOE_{ref} [-]**
short-term	0.04	25
medium-term	0.013	75
long-term	0.007	150

Acceptable exposure scenarios (including method of calculation)

Professional users	no acceptable risk for professional users
Non-professional users	acceptable risk for dust barrier treatment.
Indirect exposure as a result of use	not relevant, always lower than operator exposure Indirect exposure via food/feed for intended biocide uses in PT 18 is negligible and is consequently considered of low relevance.

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	n.a.: In inorganic chemistry, the word hydrolysis is often applied to solutions of salts and the reactions by which they are converted to new ionic species or to precipitates (oxides, hydroxides, or salts). This is not the case of the molecule SiO_2.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Based on the chemical nature of silicon dioxide Kieselguhr (inorganic structure and chemical stability of the compound: Si-O bond is highly stable), no photolytic degradation is expected.
Readily biodegradable (yes/no)	No
Biodegradation in seawater	No biodegradation: biodegradation is not applicable to inorganic substances, since these substances do not contain carbon atoms, therefore this test is not applicable for Diatomaceous Earth. Ready biodegradability studies are conducted by measuring the production of CO_2 from a test substance or the corresponding biochemical oxygen demand (BOD) which is the amount of oxygen consumed by micro-organisms when metabolising a test compound; since silicon dioxide Kieselguhr contains no carbon no CO_2 production or BOD rate could therefore be measured.
Non-extractable residues	-
Distribution in water / sediment systems (active substance)	Silicon dioxide Kieselguhr released into the environment is expected to be distributed mainly into soils and sediments and probably not at all into water or air. Due to its insolubility and density, Diatomaceous Earth will undergo sedimentation if it enters natural water bodies. Diatomaceous Earth (mainly contains amorphous silica) is expected to combine indistinguishably with the soil or sediment due to their similarity with inorganic soil/sediment matter. Diatomaceous Earth is a natural sediment.
Distribution in water / sediment systems (metabolites)	n. a. (no metabolites)

Route and rate of degradation in soil

Mineralization (aerobic)	Soils contain up to 95 % SiO_2. Al_2O_3, Fe_2O_3 and clay minerals are most common in soils. Silicon dioxide Kieselguhr itself may even be a natural component of some soils or rather build up own soil horizons (Soil Survey Staff 1997; Poetsch 2004). Based on the chemical nature of silicon dioxide Kieselguhr (inorganic structure and chemical stability of the main compound: Si-O bond is highly stable), no photo- or chemical degradation is expected, nor biodegradation (no carbon atoms are contained in the molecule). Therefore, no dissipation of silicon dioxide Kieselguhr is expected in soil. Silicon dioxide Kieselguhr used for filtration in

	brewing or wine-making is brought out as fertilizer on the fields after usage since decades without any negative effects. Further tests on stability and accumulation in soil, adsorption and mobility are not deemed necessary.
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic): -
	DT_{90lab} (20°C, aerobic): -
	DT_{50lab} (10°C, aerobic): -
	DT_{50lab} (20°C, anaerobic): -
	degradation in the saturated zone: -
Field studies (state location, range or median with number of measurements)	DT_{50f}: -
	DT_{90f}: -
Anaerobic degradation	n. a.
Soil photolysis	n. a.
Non-extractable residues	n. a.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	n. a.
Soil accumulation and plateau concentration	n. a.

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	n. a.

Fate and behaviour in air

Direct photolysis in air	No photolysis No studies have been conducted to investigate the fate and behaviour of silicon dioxide Kieselguhr in the air. Since the vapour pressure of silicon dioxide Kieselguhr is negligible, air is not a relevant compartment. Considering its physicochemical properties (non-soluble, high density, and negligible vapour pressure), silicon dioxide Kieselguhr released into the environment is expected to be distributed mainly into soil and sediment. Furthermore, its main component, amorphous silica, is a stable molecule and therefore it is not expected to be subjected to chemical transformations.
Quantum yield of direct photolysis	n. a.
Photo-oxidative degradation in air	Latitude: n. a. Season: .... DT_{50} ....
Volatilization	Non volatile

Monitoring data, if available

Soil (indicate location and type of study)	n. a.
Surface water (indicate location and type of study)	n. a.: The German commission of the evaluation of water polluting substances has classified silicon dioxide as non-hazardous to waters (Catalogue of Substances Hazardous to Water, Annex 1: list of substances not hazardous to waters, published by Umweltbundesamt 1999).
Ground water (indicate location and type of	n. a.: The German commission of the evaluation

study)	of water polluting substances has classified silicon dioxide as non-hazardous to waters (Catalogue of Substances Hazardous to Water, Annex1: list of substances not hazardous to waters, published by Umweltbundesamt 1999).
Air (indicate location and type of study)	n. a., the dust will settle down

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss (Rainbow trout)	96-hour static test	Mortality, symptoms of intoxication	OECD 203 (1992) No toxicity in the limit concentration of 100 mg a.s./l; LC_0 ≥ 100 mg a.s./l LC_{50} > 100 mg a.s./l LC_{100} > 100 mg a.s./l Schneider (2006)
Invertebrates			
Daphnia magna	48-hours static	Immobility	OECD 202 (2004) No toxic effect in the limit concentration of 100 mg a.s./l; EC_0 ≥ 100 mg a.s./l EC_{50} > 100 mg a.s./l EC_{100} > 100 mg a.s./l Vinken (2006a)
Algae			
Desmodesmus subspicatus	72 h	Growth inhibition	OECD 201 (2006) No toxic effect in the limit concentration of 100 mg a.s./l; NOE_rC ≥ 100 mg a.s./l NOE_bC ≥ 100 mg a.s./l E_rC_{50} > 100 mg a.s./l E_bC_{50} > 100 mg a.s./l Vinken (2006b)
Microorganisms			
Activated sludge	3 hours	Respiration inhibition	OECD 209 (1984) NOEC = 1000 mg a.s./l EC_{20} > 1000 mg a.s./l EC_{50} > 1000 mg a.s./l EC_{80} > 1000 mg a.s./l Reis (2006)

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworms	No acute toxicity. Experiments at a German university revealed that up to 30 Vol. % silicon dioxide Kieselguhr in soils does not harm earthworms. Soils in general contain up to 95% SiO2.
Reproductive toxicity to earthworms	No reproductive toxicity. Experiments at a German university revealed that up to 30 Vol. % silicon dioxide Kieselguhr in soils does not harm earthworms. Soils in general contain up to 95% SiO_2.

Effects on soil micro-organisms

Nitrogen mineralization	n. a. Silicon dioxide Kieselguhr is a natural raw material which chemically mainly contains silica (60-97% SiO_2). The remainder chiefly are alumina as Al_2O_3, Fe_2O_3 and alkali from clay. As natural soils contain up to 95% SiO_2. Al_2O_3, Fe_2O_3 and clay minerals are most common in soils the use of silicon dioxide Kieselguhr has no effect on soil microflora.
Carbon mineralization	n. a. Silicon dioxide Kieselguhr is a natural raw material which chemically mainly contains silica (60-97% SiO_2). The remainder chiefly are alumina as Al_2O_3, Fe_2O_3 and alkali from clay. As natural soils contain up to 95% SiO_2. Al_2O_3, Fe_2O_3 and clay minerals are most common in soils the use of silicon dioxide Kieselguhr has no effect on soil microflora.

Effects on terrestrial vertebrates

Acute toxicity to mammals	n. a., SiO_2 is a food and feed additive without acute toxicity
Acute toxicity to birds	n. a., SiO_2 is a food and feed additive without acute toxicity
Dietary toxicity to birds	n. a., SiO_2 is a food and feed additive without dietary toxicity
Reproductive toxicity to birds	n. a., SiO_2 is a food and feed additive without reproductive toxicity

Effects on honeybees

Acute oral toxicity	The application range of silicon dioxide Kieselguhr as biocide excludes a contact to honey bees.
Acute contact toxicity	The application range of silicon dioxide Kieselguhr as biocide excludes a contact to honey bees.

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	The application range of silicon dioxide Kieselguhr as biocide excludes a contact to beneficial arthropods.
Acute contact toxicity	The application range of silicon dioxide Kieselguhr as biocide excludes a contact to beneficial arthropods.
Acute toxicity to …………………………………..	The application range of silicon dioxide Kieselguhr as biocide excludes a contact to beneficial arthropods.

Bioconcentration

Bioconcentration factor (BCF)	n. a. Silicon dioxide Kieselguhr is chemically inert. It is not soluble – neither in water, nor in lipids and has no lipophilic properties. Furthermore, it is used indoor. Thus, Silicon dioxide Kieselguhr has no potential for bioaccumulation.
Depuration time (DT_{50}) (DT_{90})	n. a.
Level of metabolites (%) in organisms accounting for > 10 % of residues	n. a.

Appendix II: List of Intended Uses

Summary of intended uses[13]

Object and/or situation (a)	Member State or Country	Product name	Organisms controlled (c)	Formulation Type (d-f)	Formulation Conc. of as (i)	Application method kind (f-h)	Application number min max (k)	Application interval between applications (min)	Applied amount per treatment g as/L min max	Applied amount per treatment water L/m² min max	Applied amount per treatment g as/m² min max	Remarks: (m)
Poultry Pens	Germany, Austria, Italy, Spain, France, UK, Sweden, Norway, Denmark, Finland	Insecto Sec	Poultry Mite	CP	100 % DE	Application by professional operators for the control of poultry red mites in poultry pens The representative product INSECTOSEC is a dustable powder which is applied as dry dust with a handheld bellow, electrostatic dusters and dusting guns with compressed air against poultry mites	3	Application at D0, D7 and D21	n. a.	n. a.	50	InsectoSec gets applied as a dry dust. Relative ambient humidity should not exceed 75%.
Private households, food/ feed processing industry facilities, glasshouses etc.	As above	As above	Black ant, Silverfish, Wood louse	CP	As above	Application by professional operators for the control of arthropods in food and feed processing industry or storage facilities	1		n. a.	n. a.	Lines of 0.5-2 cm width and app. 2 mm hight correspo	10 g/m² (complete surface - area and walls - to be added up). InsectoSec gets applied as a dry dust.

[13] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998.

						The representative product INSECTOSEC is a dustable powder which is applied as dry dust dusting guns with compressed air. Application by non-professionals for the control of arthropods in private households by pouring dust barriers. The representative product INSECTOSEC is a dustable powder which is applied by a dust barrier against Black ant, Silverfish, Wood louse					nding to 5 g/m	Relative ambient humidity should not exceed 75%. Dust barriers to prevent insects to enter into certain areas should have 0.5-2 cm width and app. 2 mm hight, corresponding to 5 g/m.
			Cat flea			Application by non-professionals for the control of arthropods in private households by crack and crevice treatment The representative product INSECTOSEC is a dustable powder which is applied by a surface treatment against cat fleas	1				10 g/m²	

a) *e.g.* biting and suckling insects, fungi, molds;
(b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained

(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A2.9/01 also filed 3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A2.10.2/01 also filed A3.1.3/02 also filed A3.17/01 also filed A7.1.1.1.1/01 also filed A7.1.1.1.2/01 also filed A7.2/02	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. U. S. Department of the Interior, U. S. Geological Survey Date: 2003	-	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A2.10.2/02	IARC	1997	Silica, Crystalline silica-inhaled in the form of quartz or cristobalite from occupational sources (Group 1), Amorphous silica (Group 3). Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization. International Agency for Research on Cancer, Monographs Vol. 68 p. 41-50.	-	-	No	Yes	No	-	NO
A3.1.1/01 also filed A3.1.2/01 also filed A3.11/01	International Program on Chemical Safety	2001	International Chemical Safety Card Diatomaceous earth (uncalcined). Date: March 2001	International Program on Chemical Safety (IPCS)	0248	No	Yes	No	-	NO
A3.1.2/01 also filed A3.1.1/01 also filed A3.11/01	International Program on Chemical Safety	2001	International Chemical Safety Card Diatomaceous earth (uncalcined). Date: March 2001	International Program on Chemical Safety (IPCS)	0248	No	Yes	No	-	NO
A3.1.3/01 also filed A7.1.2/02	Anderson, A.R.	1990	Diatomaceous earth occurrence in Nova Scotia. Economic Geology Series 90-1 Date: 1990	Department of Mines and Energy, Halifax, Nova Scotia, USA	-	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.1.3/02 also filed A2.10.2/01 also filed A3.17/01 also filed A7.1.1.1.1/01 also filed A7.1.1.1.2/01 also filed A7.2/02	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. Date: 2003	U. S. Department of the Interior, U. S. Geological Survey	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	NO
A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.1/02 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	NO
A3.3/01 also filed 2.9/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.4/01 also filed 2.9/01 also filed A3.3/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A3.4/02 also filed A3.7/01 also filed A3.9/02 also filed A3.11/02 also filed A7.1.1.1.1/02 also filed A7.1.1.1.2/02	Berufsgenossenschaft der keramischen Glas-Industrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossen-schaft der keramischen Glasindustrie	-	No	Yes	No	-	NO
A3.4/03	XXXX	2009	Analytical report. XXXX	Chemische Produkt-Beratung und -Analyse GmbH (CBA), Kirkel-Limbach, Germany	XXXX	No	No	Yes	Biofa AG	YES
A3.4/04 also filed A3.10/01	XXXX	2009	Thermal stability of Diatomaceous earth XXXX	SGS Institut Fresenius GmbH, Dresden, Germany	XXXX	No	No	Yes	Biofa AG	YES

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.4/05	XXXX	2012	Analysis Report NMR. XXXX	Currenta GmbH & Co. OHG, Leverkusen, Germany	None	No	No	Yes	Biofa AG	YES
A3.5/01 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A3.5/02 also filed A3.2/01 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.1/02 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	-	No	Yes	No	-	NO
A3.5/03	XXXX	2010a	Final test Report: Water solubility test according to OECD 105 and solubility in two organic solvents of Diatomeenerde. XXXX	Steinbeis-Transferzentrum Angewandte und Umweltchemie, Reutlingen, Germany	XXXX	Yes	No	Yes	Biofa AG	YES

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.6/01 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A3.7/01 also filed A3.4/02 also filed A3.9/02 also filed A3.11/02 also filed A7.1.1.1.1/02 also filed A7.1.1.1.2/02	Berufsgenossenschaft der keramischen Glas-Industrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossenschaft der keramischen Glasindustrie	-	No	Yes	No	-	NO
A3.7/02	XXXX	2010b	Solubility test in two organic solvents according to OECD-Guideline 105 of Diatomeenerde. XXXX	Steinbeis-Transferzentrum Angewandte und Umwelt-Chemie, Reutlingen, Germany	XXXX	Yes	No	Yes	Biofa AG	YES

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.9/01 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A3.9/02 also filed A3.4/02 also filed A3.7/01 also filed A3.11/02 also filed A7.1.1.1.1/02 also filed A7.1.1.1.2/02	Berufsge-nossenschaft der kerami-schen Glas-Industrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossen-schaft der keramischen Glasindustrie	-	No	Yes	No	-	NO
A3.10/01 also filed A3.4/04	XXXX	2009	Thermal stability of Diatomaceous earth (after OECD guideline 113). XXXX	SGS Institut Fresenius GmbH, Dresden, Germany	XXXX	No	No	Yes	Biofa AG	YES
A3.11/01 also filed A3.1.1/01 also filed A3.1.2/01	International Program on Chemical Safety	2001	International Chemical Safety Card Diatomaceous earth (uncalcined). Date: March 2001	International Program on Chemical Safety (IPCS)	0248	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.11/02 also filed A3.4/02 also filed A3.7/01 also filed A3.9/02 also filed A7.1.1.1.1/02 also filed A7.1.1.1.2/02	Berufsge-nossenschaft der kerami-schen Glas-Industrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossen-schaft der keramischen Glasindustrie	-	No	Yes	No	-	NO
A3.11/03 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO
A3.13/01 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A3.17/01 also filed A2.10.2/01 also filed A3.1.3/02 also filed A7.1.1.1.1/01 also filed A7.1.1.1.2/01 also filed A7.2/02	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. Date: 2003	U. S. Department of the Interior, U. S. Geological Survey	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	NO
A3.18/01	XXXX	2013	Determination of the particle size distribution of five batches of InsectoSec. XXXX	Eurofins Agroscience Services, Niefern-Öschelbronn, Germany	XXXX	Yes	No	Yes	Biofa AG	YES
A3.18/02	XXXX	2013	Surface analysis of Kieselguhr (Diatomeceous earth) samples. XXXX	Intertek Pharmaceuticals Services Manchester, Manchester, UK	XXXX	Yes	No	Yes	Biofa AG	YES
A4.2/01 also filed A2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	NO

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A4.2/02	NIOSH (Ed.)	2003a	Silica, crystalline, by XRD (filter redeposition). *NIOSH Manual of Analytical Methods (NMAM), fourth Edition* Date: 2003-03-15	National Institute for Occupational Safety and Health, USA	Method No. 7500, Issue 4	No	Yes	No	-	NO
A4.2/03	NIOSH (Ed.)	2003b	Silica, amorphous. *NIOSH Manual of Analytical Methods (NMAM), fourth Edition* Date: 2003-03-15	National Institute for Occupational Safety and Health, USA	Method No. 7501, Issue 3	No	Yes	No	-	NO
A5.3.1/01	XXXX	2011a	Efficacy of InsectoSec® against Mites (*Dermanyssus gallinae*) in laboratory trails. XXXX	ZeckLab, Burgwedel, Germany	No Report No.	No	No	Yes	Biofa AG	Y
A5.3.1/02	XXXX	2011b	Field Studies to Evaluate InsectoSec® against Poultry Red Mites (*Dermanyssus gallinae*). XXXX	ZeckLab, Burgwedel, Germany	No Report No.	No	No	Yes	Biofa AG	Y
A5.3.1/03	XXXX	2009	Biological test report: Efficacy of a product against various crawling species. Efficacy of product Insecto Sec® against fleas, woodlice, silverfish and ants. XXXX	BioGenius GmbH, Biology, Bergisch-Gladbach, Germany	XXXX	No	No	Yes	Biofa AG	Y

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A5.3.1/04	XXXX	2011	Efficacy of product InsectoSec® against cat fleas. XXXX	BioGenius GmbH, Biology, Bergisch-Gladbach, Germany	XXXX	No	No	Yes	Biofa AG	Y
A5.4.1	Reißner, S.	2009	Diatomaceous earth, mode of action Date: 2009-10-01	Biofa AG	-	No	-	No	Biofa AG	Y
A6.1.1/01 also filed A6.1.2/01 also filed A6.1.4/01	XXXX	1958a	Progress Report, Subject: Acute Oral Administration, Acute Dermal Application, Acute Eye Application, Acute Inhalation Exposure XXXX	XXXX	-	No	No	Yes	Biofa AG	N
A6.1.1/02 also filed A6.1.4/02	XXXX	1979	Final Report. Acute oral, dermal and ocular toxicities in the rat of Dryacide.	XXXX	-	No	No	Yes	Dr. Schaette AG	Y
A6.1.1/03 also filed A3.2/01 also filed A3.5/02 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.1/02 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	N

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A6.1.1/04	Subramanyam Bh., Swanson C.L., Madamanchi N. and Norwood S.	1994	Effectiveness Of Insecto®, A New Diatomaceous Earth Formulation, In Suppressing Several Stored-Grain Insect Species. Proceedings of the 6th International Conference on Stored-Product Protection, Canberra, Australia, 650. Ed. E. Highley, E. J. Wright, H. J. Banks and B.R. Champ, Vol. 2, pp 650-659. University Press, Cambridge, U.K.	-	-	No	Yes	No	-	N
A6.1.2/01 also filed A6.1.1/01 also filed A6.1.4/01	XXXX	1958a	Progress Report, Subject: Acute Oral Administration, Acute Dermal Application, Acute Eye Application, Acute Inhalation Exposure XXXX	XXXX	-	No	No	Yes	Biofa AG	N
A6.1.3/01	XXXX	1980	Acute inhalation toxicity in the rat.	XXXX	-	No	No	Yes	Biofa AG	Y
A6.1.4/01 also filed A6.1.1/01 also filed A6.1.2/01	XXXX	1958a	Progress Report, Subject: Acute Oral Administration, Acute Dermal Application, Acute Eye Application, Acute Inhalation Exposure XXXX	XXXX	-	No	No	Yes	Biofa AG	N
A6.1.4/02 also filed A6.1.1/01	XXXX	1979	Final Report. Acute oral, dermal and ocular toxicities in the rat of Dryacide.	XXXX	-	No	No	Yes	Biofa AG	Y

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A6.1.5	Brandenberger *et al.*	2013	Engineered silica nanoparticles act as adjuvants to enhance allergic airway disease in mice. Part Fibre Toxicol. 2013 Jul 1;10:26.	-	-	N	Y	N	-	N
A6.1.5	Park *et al.*	2015	Acute exposure to silica nanoparticles aggravate airway inflammation: different effects according to surface characteristics. Exp Mol Med. 2015 Jul 17;47:173.	-	-	N	Y	N	-	N
A6.1.5	Watanabe *et al.*	2015	Association of Sand Dust Particles with Pulmonary Function and Respiratory Symptoms in Adult Patients with Asthma in Western Japan Using Light Detection and Ranging: A Panel Study. Int J Environ Res Public Health. 2015 Oct 16;12(10):13038-52.	-	-	N	Y	N	-	N
A6.2/01	XXXX	2006	Determination of grain size distribution. XXXX	KI Keramik-Institut GmbH, Meißen, Germany	-	No	No	Yes	Biofa AG	N
A6.3.1/01	XXXX	1958b	Final Report. Subacute Feeding in rats.	XXXX	-	No	No	Yes	Biofa AG	Y

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A6.3.1/02	XXXX	1980	Report on the effect of Dryacide on feed intake by sheep.	XXXX	-	No	No	Yes	Biofa AG	N
A6.3.1/03 also filed 2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A7.1.2/01 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	N
A6.3.2/01 also filed A6.4.2/01	OECD SIDS	2004	SIDS Initial Assessment Report for SIAM 19, Silicon dioxide (synthetic amorphous silica).	-	-	No	Yes	No	-	N
A6.3.3/01	Arts, J.H.E., Muijser H., Duistermaat E., Junker K., and Kuper C.F.	2007	Five-day inhalation toxicity study of three types of synthetic amorphous silicas in Wistar rats and post-exposure evaluations for up to 3 months. Food Chem. Toxicol. **45**(10), pp. 1856-67	TNO Quality of Life, Zeist, The Netherlands	-	No	Yes	No	-	N

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A6.3.3/02	XXXX ,	2015	A 28-Day Inhalation Toxicity Study of Diatomaceous Earth in Sprague Dawley Rats with a 4-Week Recovery. XXXX	XXXX	XXXX	Yes	No	Yes	Biofa AG	Y
A6.4.1/01	Bertke, E.M.	1964	The effect of ingestion of diatomaceous earth in white rats; a subacute toxicity test. Toxicology of Applied Pharmacolology 6:284-291	Division of Life Science, Arizona State University, Tempe, Arizona	-	No	Yes	No	-	Y
A6.4.2/01 also filed A6.3.2/01	OECD SIDS	2004	SIDS Initial Assessment Report for SIAM 19, Silicon dioxide (synthetic amorphous silica).	-	-	No	Yes	No	-	N
A6.4.3/01	Reuzel, P.G.J., Bruijntjes J.P., Feron V.J. and Woutersen R.A.	1991	Subchronic Inhalation Toxicity of Amorphous Silicas and Quartz Dust in Rats. Fd. Chem. Toxic. Vol. 29, no. 5, pp. 341-354	TNO Toxicology and Nutrition Institute, Zeist, The Netherlands	-	No	Yes	No	-	N

(Sub)Section / Annex point	Author(s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner	Essential for the evaluative (yes/no)
A6.4.3/02 also filed A6.6.4/01	Johnston, C. J., Driscoll K.E., Finkelstein J.N., Baggs R., O´Reilly M.A., Carter J., Gelein R., Oberdörster G.	2000	Pulmonary Chemokine and Mutagenic Responses in Rats after Subchronic Inhalation of Amorphous and Crystalline Silica. Toxicological Sciences 56, 405-413	Department of Environmental Medicine and Pediatrics, The University of Rochester, New York, USA and Procter and Gamble Pharmaceutical, Health Care Research Center, Ohio, USA	-	No	Yes	No	-	N
A6.4.3/03 also filed A6.5/01	Schepers, G. W. H.	1981	Biological action of precipitation-process submicron amorphous silica (HI-SIL 233). In: Dunnom, D. D., ed.: Health effects of synthetic silica particulates: ASTM STP 732. American Society for Testing and Materials; pp. 144-173; ASTMspecial technical publication 732 GLP not known, published	-	-	No	Yes	No	-	N
A6.4.3/04 also filed A6.5/04 also filed A6.12.1/03 also filed A6.12.4/01	EPA	1996	Ambient Levels and Noncancer Health Effects of Inhaled Cristalline and Amorphous Silica: Health Issue Assessment.	United States Environmental Protection Agency, Washington, DC, USA	EPA/600/R-95/115	No	Yes	No	-	N

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A6.4.3/05 also filed A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.5/05 also filed A6.12.1/02 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	N
A6.5/01 also filed A6.4.3/03	Schepers, G. W. H.	1981	Biological action of precipitation-process submicron amorphous silica (HI-SIL 233). In: Dunnom, D. D., ed.: Health effects of synthetic silica particulates: ASTM STP 732. American Society for Testing and Materials; pp. 144-173; ASTMspecial technical publication 732	-	-	No	Yes	No	-	N
A6.5/02 also filed A6.2/01	XXXX	2006	Determination of grain size distribution.	KI Keramik-Institut GmbH, Meißen, Germany	XXXX	No	No	Yes	Biofa AG	N
A6.5/03	Pratt, P.C.	1983	Lung dust content and response in guinea pigs inhaling three forms of silica. Arch. Environ. Health 38: 197-204.	-	-	No	Yes	No	-	N

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A6.5/04 also filed A6.4.3/04 also filed A6.12.1/03 also filed A6.12.4/01	EPA	2006	Ambient Levels and Noncancer Health Effects of Inhaled Cristalline and Amorphous Silica: Health Issue Assessment.	United States Environmental Protection Agency, Washington, DC, USA	EPA/600/R-95/115	No	Yes	No	-	N
A6.5/05 also filed A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.12.1/02 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	N
A6.5/06	Volk, H.	1960	The Health of Workers in a Plant Making Highly Dispersed Silica.	Degussa, Rheinfelden, Germany	*Archives of Environmental Health* **1**, 47-50	N	Y	N	1.	2.
A6.5/07	Groth, D.H. et al.	1981	Chronic Effects of Inhaled Amorphous Silicas in Animals. *Health Effects of Synthetic Silica Particulates, ASTM STP 732*, D.D. Dunnom, Ed., , pp. 118-143	American Society for Testing and Materials	-	No	Yes	No	-	N

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A6.6.1/01 also filed A6.8.2/01	Lewinson, J., Mayr, W. and Wagner, H.	1994	• Characterization and toxicological behavior of synthetic amorphous hydrophobic silica. Regul. Toxicol Pharmacol 20, 37-57	Degussa Corporation, Ridgefield Park, New Jersey, USA and Degussa AG, Hanau, Germany	-	No	Yes	No	-	N
A6.6.1/02	Prival, M.J. et al.	1991	• Bacterial mutagenicity testing of 49 food ingredients gives very few positive results. • Mutat Res. 1991 Aug; **260**(4):321-9	-	-	No	Yes	No	-	N
A6.6.2/01	Zhong, B., Whong, W. and Ong, T.	1997	• Detection of mineral-dust-induced DNA damage in two mammalian cell lines using the alkaline single cell gel/ comet assay. • Mutation Research 393, 181-187.	National Institute for Occupational Safety and Health, Health Effects Laboratory Division, Morgantown, USA	-	No	Yes	No	-	N
A6.6.2/02	Hart, G.A. and Hesterberg, T.W.	1998	In vitro toxicity of respirable-size particles of diatomaceous earth and crystalline silica compared with asbestos and titanium dioxide. *JOEM*, Vol. 40, No. 1, pp. 29-42	Johns Manville Corporation Technical Center, Littleton, CO, USA	-	No	Yes	No	-	N

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A6.6.4/01 also filed A6.4.3/02	Johnston, C. J., Driscoll K.E., Finkelstein J.N., Baggs R., O´Reilly M.A., Carter J., Gelein R., Oberdörster G.	2000	Pulmonary Chemokine and Mutagenic Responses in Rats after Subchronic Inhalation of Amorphous and Crystalline Silica. Toxicological Sciences 56, 405-413	Department of Environmental Medicine and Pediatrics, The University of Rochester, New York, USA and Procter and Gamble Pharmaceutical, Health Care Research Center, Ohio, USA	-	No	Yes	No	-	N
A6.6.5/01	XXXX	2015	The alkaline in vivo Comet Assay with Diatomaceous Earth / Diatomaceous silica in lung and stomach of Wistar Han Rats after intra-tracheal dosing. XXXX	XXXX	XXXX	Yes	No	Yes	Biofa AG	Y
A6.7/01	XXXX	2006	Analysis of Diatomaceous Earth. XXXX	SGS Institut Fresenius, CTS Spezielle Analytik. Taunusstein, Germany	-	No	No	Yes	Biofa AG	N
A6.8.1/01	Morgareidge, K.	1973a	Teratologic evaluation of FDA 71-48 (Syloid; Silica aerogel) in rats. Date: 1973-05-01	Food and Drug Research Laboratories, Inc., Maspeth, NY, USA	Project No. FDA 71-260	No	Yes	No	-	Y

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A6.8.1/02	Morgareidge, K.	1973b	Teratologic evaluation of FDA 71-48 (Syloid; Silica aerogel) in rabbits. Date: 1973-09-05	Food and Drug Research Laboratories, Inc., Maspeth, NY, USA	Project No. FDA 71-260	No	Yes	No	-	Y
A6.8.2/01 also filed A6.6.1/01	Lewinson, J., Mayr, W. and Wagner, H.	1994	• Characterization and toxicological behavior of synthetic amorphous hydrophobic silica. Regul. Toxicol Pharmacol 20, 37-57	Degussa Corporation, Ridgefield Park, New Jersey, USA and Degussa AG, Hanau, Germany	-	No	Yes	No	-	N
A6.10/01	O'Reilly, K.M.A. et al.	2005	Crystalline and amorphous silica differentially regulate the cyclooxygenase-prostaglandin pathway in pulmonary fibroblasts: implications for pulmonary fibrosis.	-	*Am J Physiol Lung Cell Mol Physiol. 288(6):L 1010-6*	No	Yes	No	-	N
A6.12.1/01	Rafnsson, V. and Gunnarsdottir H.	1997	Lung cancer incidence among Iceland cohort exposed to diatomaceous earth and cristobalite. Scand J Work Environ Health 23 (3): 187-92	-	-	No	Yes	No	-	N
A6.12.1/02 also filed A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.2/01 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	N

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A6.12.1/03 also filed A6.4.3/04 also filed A6.5/04 also filed A6.12.4/01	EPA	1996	Ambient Levels and Noncancer Health Effects of Inhaled Cristalline and Amorphous Silica: Health Issue Assessment.	United States Environmental Protection Agency, Washington, DC, USA	EPA/600/ R-95/115	No	Yes	No	-	N
A6.12.2/01 also filed A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.1/02 also filed A7.2/04	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet. nlm.nih.gov)	Databank number 682	No	Yes	No	-	N
A6.12.4/01 also filed A6.4.3/04 also filed A6.5/04 also filed A6.12.1/03	EPA	1996	Ambient Levels and Noncancer Health Effects of Inhaled Cristalline and Amorphous Silica: Health Issue Assessment.	United States Environmental Protection Agency, Washington, DC, USA	EPA/600/ R-95/115	No	Yes	No	-	N
A7.1.1.1.1/01 also filed A2.10.2/01 also filed A3.1.3/02 also filed A3.17/01 also filed A7.1.1.1.2/01 also filed A7.2/02	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. U. S. Department of the Interior, U. S. Geological Survey Date: 2003	-	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	YES

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A7.1.1.1.1/02 also filed A3.4/02 also filed A3.7/01 also filed A3.9/02 also filed A3.11/02 also filed A7.1.1.1.2/02	Berufsge-nossenschaft der keramischen Glasindustrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossen-schaft der keramischen Glasindustrie	-	No	Yes	No	-	YES
A7.1.1.1.2/01 also filed A2.10.2/01 also filed A3.1.3/02 also filed A3.17/01 also filed A7.1.1.1.1/01 also filed A7.2/02	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. U. S. Department of the Interior, U. S. Geological Survey Date: 2003	-	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	YES
A7.1.1.1.2/02 also filed A3.4/02 also filed A3.7/01 also filed A3.9/02 also filed A3.11/02 also filed A7.1.1.1.1/02	Berufsge-nossenschaft der keramischen Glasindustrie (Ed.)	2006	Amorphe Kieselsäuren.	Berufsgenossen-schaft der keramischen Glasindustrie	-	No	Yes	No	-	YES

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A7.1.2/01 also filed A2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	YES
A7.1.2/02 also filed A3.1.3/01	Anderson, A.R.	1990	Diatomaceous earth occurrence in Nova Scotia. Economic Geology Series 90-1 Date: 1990	Department of Mines and Energy, Halifax, Nova Scotia, USA	-	No	Yes	No	-	YES
A7.2/01 also filed A2.9/01 also filed A3.3/01 also filed A3.4/01 also filed A3.5/01 also filed A3.6/01 also filed A3.9/01 also filed A3.11/03 also filed A3.13/01 also filed A4.2/01 also filed A6.3.1/03 also filed A7.1.2/01	Korunic, Z.	1998	Diatomaceous earth, a group of natural insecticides. Journal of Stored Product Research, Vol. 34, No. 2/3, pp. 87 –97.	Hedley Technologies Inc., Mississauga, Ontario, USA	-	No	Yes	No	-	YES

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A7.2/02 also filed A2.10.2/01 also filed A3.1.3/02 also filed A3.17/01 also filed A7.1.1.1.1/01 also filed A7.1.1.1.2/01	Moyle, P.R. and Dolley, T.P.	2003	With or without Salt – a Comparison of Marine and Continental-Lacrustine Diatomite Deposits. Chapter D of Contributions to Industrial-Minerals Research. U. S. Department of the Interior, U. S. Geological Survey Date: 2003	-	Bulletin 2209 –D, Version 1.0	No	Yes	No	-	YES
A7.2/03	XXXX	2006	5 Batch Analysis. XXXX	Terrachem GmbH, Analysenlabor, Mannheim, Germany	XXXX	No	No	Yes	Biofa AG	YES
A7.2/04 also filed A3.2/01 also filed A3.5/02 also filed A6.1.1/03 also filed A6.4.3/05 also filed A6.5/05 also filed A6.12.1/02 also filed A6.12.2/01	Hazardous Substances Data Bank	2006	Amorphous Silica. Date: 2006-03-04	Database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov)	Databank number 682	No	Yes	No	-	YES
A7.2/05	Scheffer, F. and Schachtschabel, P. (Ed.)	1992	Lehrbuch der Bodenkunde. Chapter VI. Mineralzusammensetzung von Böden und Mineralbestimmung.	Ferdinand Enke-Verlag, Stuttgart, Germany	-	No	Yes	No	-	NO

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A7.2/06	Soil Survey Staff	1997	Keys to Soil Taxonomy. Chapter 3 Horizons and properties diagnostics for the higher categories: organic soils. Pocahontas Press, Inc.	Soil Survey Staff, Soil Conservation Service, U.S Department of Agriculture	-	No	Yes	No	-	YES
A7.2/07	Poetsch, T.	2004	Forms and dynamics of silica gel in a tuff-dominated soil complex: Results of micromorphological studies in the Central Highlands of Mexico. *Revista Mexicana de Ciencias Geológicas, v. 21, núm. 1, 2004, p. 195-201*	Universität Hamburg, Institut für Geographie, Hamburg, Germany	-	No	Yes	No	-	YES
A7.4.1.1/01	XXXX	2006	Acute Toxicity of Diatomaceous Earth to Rainbow Trout (*Oncorhynchus mykiss*) in a 96-hour Static Test	XXXX	XXXX	Yes	No	Yes	Biofa AG	YES
A7.4.1.2/01	XXXX	2006a	Acute Toxicity of Diatomaceous Earth to *Daphnia magna* in a Static 48-hour Immobilization Test	Ibacon GmbH, Rossdorf, Germany	XXXX	Yes	No	Yes	Biofa AG	YES
A7.4.1.3/01	XXXX	2006b	Toxicity of Diatomaceous Earth to *Desmodesmus subspicatus* in an Algal Growth Inhibition Test	Ibacon GmbH, Rossdorf, Germany	XXXX	Yes	No	Yes	Biofa AG	YES
A7.4.1.4/01	XXXX	2006	Toxicity of Kieselguhr (Diatomaceous Earth) to Activated Sludge in a Respiration Inhibition Test	Ibacon GmbH, Rossdorf, Germany	XXXX	Yes	No	Yes	Biofa AG	YES