Phototransformation in air

Guideline / Test Method	Initial Molar TS concentration	Total Recovery of Test Substance [% of appl. a.s.]	Photolysis rate constant (k^c_p)	Direct photolysis sunlight rate constant (K_{pE})	Reaction quantum yield (0^c_E)	Half-life ($t_{1/2E}$)	Remarks	Reference
N/A	N/A	N/A	N/A	N/A	N/A	N/A	Phototransformation in air (estimation method), including identification of breakdown products: Silicon dioxide is not volatile, and therefore exposure via the atmospheric compartment is not considered relevant. Notwithstanding the above, the structure of silicon dioxide is O=Si=O. This structure means that OH-radicals are unlikely to be generated during degradation in air. When pseudo-first order rate constant for degradation in air was estimated using the QSAR method, the rate constant was zero. This result supports the above statement that OH radicals are unlikely to be generated during degradation of silicon dioxide in air. Silicon dioxide will not have an impact on global warming because it does not exist in the gaseous state at ambient temperature and pressure. The presence of absorption bands in the IR spectrum region 800-1200nm is therefore not applicable. It is also highly unlikely that silicon dioxide will have any impact either on ozone depletion in the stratosphere or ozone formation in the troposphere. This is because silicon dioxide does not contain chlorine substituents, and OH radicals are unlikely to be generated during degradation of silicon dioxide in air. The final atmospheric risk indicator is acidification. As silicon dioxide does not contain Cl, F, N or S substituents, acidification is not considered to be a risk to receiving soil or surface water.	Document IIIA, Section 7.3.1

Footnote

Further studies to determine fate and behaviour of silicon dioxide in the air (Document IIIA, Section 7.3.2) are not considered necessary because The "TNsG" states that further studies are required to determine fate and behaviour in air if: The active substance is to be used in fumigant preparations and the active substance causes risk to the atmospheric compartment. Silicon dioxide is not intended for use as a fumigant. As shown in Document IIIA, Section 7.3.1 the preliminary risk assessment for exposure to the atmosphere does not indicate the requirement for additional studies. Therefore further studies have not been submitted.

4.1.1.3 Distribution

Absorption onto/desorption from soils (1 of 4)

Guideline /test method	Absorbed a.s. [%]	K_a [1]	K_{aOC} [2]	K_d [3]	K_{dOC} [4]	K_a / K_d [5]	Degradation products		Remarks	Reference
							Name	[%] of a.s.		
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Amorphous silicon dioxide is not expected to reach the soil compartment (see Document IIIA, Section 2.10 for exposure assessment) and there are no indications that it will bioaccumulate (see Document IIIA, Section 7.4.2 and Section 2.10 for further details). Also a value for log K_{oc} can be calculated. In the *Technical Guidance Document on Risk Assessment in support of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market*, (TGD) Chapter 3, it states that K_{oc} can be estimated using K_{ow} for non-ionic substances using QSARS. Log K_{ow} has been calculated for silicon dioxide to be 0.53 (see Document IIIA, Section 3.9 for calculation). Using LOGKOW as the most appropriate QSAR from Table 4, Page 26, Chapter 4 of the TGD gives the equation for the estimation of log K_{oc} for a non-hydrophobic substance as: log K_{oc} = 0.52 log K_{ow} + 1.02 Therefore for silicon dioxide: log K_{oc} = (0.52 x 0.53) + 1.02 = 1.30 and a standard error of 0.56 giving: log K_{oc} = 1.30 ± 0.56. As this calculation is expected to reflect a result determined by experimentation, it is not deemed scientifically necessary to perform any further studies.	Document IIIA Section 7.1.3 Document IIIA Section 7.1.4 Document IIIA Section 7.1.4.1

Footnotes

1. It is not scientifically necessary to conduct further studies on the adsorption and desorption of amorphous silicon dioxide in water sediment systems (Document IIIA, Section 7.1.4) because the preliminary risk assessment indicates it is scientifically unjustified, and not necessary due to prerequisites fulfilled on limited exposure and toxicity profile.

Amorphous silicon dioxide does not biodegrade (refer to data end points Document IIIA, Section 7.1.1.2.1 and Document IIIA, Section 7.1.1.2.2). Notwithstanding this, it is not scientifically necessary to determine the aerobic biodegradation of amorphous silicon dioxide in soil due to prerequisites fulfilled on limited exposure and toxicity profile. This is because: a. Amorphous silicon dioxide as used as an insecticide (PT18) is intended for indoor use only. b. Amorphous silicon dioxide as used as an insecticide (PT18) is not intended for direct application to the environment c. Notwithstanding the above, there is potential for exposure to the environment as a result of disposal of waste material. The risk to the environment from the act of disposal is considered to be insignificant. This is because the quantity of amorphous silicon dioxide being disposed of compared to the volume of total waste is minute. The total estimated disposal of amorphous silicon dioxide across the whole of the EU is < 0.00000073% of the total waste generated and sent to landfill in the UK alone (see Document IIA, Section 2.10 for further details). This means that any amorphous silicon dioxide that is sent for landfill is massively diluted by the large volume of municipal waste continually entering landfill sites in the UK. The data available on the environmental toxicity of amorphous silicon dioxide shows that this volume is extremely unlikely to cause any adverse effect to the environment, and as such requires no further investigation.

2. A field study on accumulation in sediment (Document IIIA, Section 7.1.4.1) has not been submitted for the following reasons: The "TNsG" states that a field trial on accumulation in the sediment is needed only if non extractable residues are formed in the initial water/sediment study submitted in Document IIIA, section 7.1.2.2.2, and these residues exceed 70% of the initial dose, or if the mineralisation rate in this study is less than 5% in 100 days. An initial water/sediment study (Document IIIA, Section 7.1.2.2.2) has not been submitted in, for the following reasons: a. The testing of the biodegradation of silicon dioxide in freshwater/sediment is scientifically unjustified because silicon dioxide, under normal conditions of use in Rentokil Initial's insecticide (PT18) products will not be applied directly or indirectly to the sediment in aquatic systems. b. Testing for the ready biodegradability (Document IIIA, Section A7.1.1.2.1) of silicon dioxide is scientifically unjustified. Silicon dioxide is an inorganic chemical, with the molecular formula O=Si=O. It is scientifically not necessary to determine the biodegradability of inorganic chemicals, because the approved EC method for ready biodegradability (EC method C4 a-f) applies only to organic compounds. In addition, the "TNsG" states that the ready biodegradation test is required of organic compounds. c. Inherent biodegradability (Document IIIA, Section A7.1.1.2.2) is technically not feasible to perform on silicon dioxide as the approved EC test methods C9 and C12 are designed to work with water-soluble, non-volatile organic substances. While silicon dioxide is slightly soluble and non-volatile, it is an inorganic compound. It is for the same reasons that it is not necessary to submit a field trial on accumulation of silicon dioxide in the sediment. Notwithstanding this, the preliminary risk assessment for exposure to water does not indicate the need to conduct additional studies on the fate and behaviour of silicon dioxide in the aquatic compartment.

Absorption onto/desorption from soils (2 of 4)

Guideline/ test method	Absorbed a.s. [%]	K_a [1]	K_{aOC} [2]	K_d [3]	K_{dOC} [4]	K_a / K_d [5]	Degradation products Name	Degradation products [%] of a.s.	Remarks	Reference
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Aerobic degradation in soil, initial study: Silicon dioxide is an inorganic chemical, with the molecular formula O=Si=O. The approved test guideline OECD 304A applies only to ^{14}C-labelled material. Therefore a test to determine the aerobic biodegradation of silicon dioxide in soil has not been submitted.	Document IIIA Section 7.2.1
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Aerobic degradation in soil, further studies: Silicon dioxide is an inorganic chemical, with the molecular formula O=Si=O and biodegradability is relevant only to organic compounds. Therefore tests to determine the aerobic degradation of silicon dioxide in soil have not been submitted. Notwithstanding this, the preliminary risk assessment for exposure to soil does not indicate the need to conduct additional studies on the fate and behaviour of silicon dioxide in the soil compartment.	Document IIIA Section 7.2.2
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Rate and route of degradation: The "TNsG" states that the rate and route of degradation including the identification of any metabolites and degradation products in at least three soil types under appropriate conditions is required only if: a. The DT_{50lab} determined in the initial aerobic degradation study in soil (Document IIIA, section 7.2.1) is more than 21 days and the PEC/PNEC >1 for soil; b. there is danger for groundwater; c. other refinement of the preliminary risk assessment for soil is necessary. Silicon dioxide is an inorganic chemical, with the molecular formula O=Si=O and the approved test guideline OECD 304A applies only to ^{14}C-labelled material. Notwithstanding the above, the preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment. Therefore an initial aerobic degradation study in soil has not been submitted.	Document IIIA Section 7.2.2.1

Absorption onto/desorption from soils (3 of 4)

Guideline/ test method	Absorbed a.s. [%]	K_a [1]	K_{aOC} [2]	K_d [3]	K_{dOC} [4]	K_a / K_d [5]	Degradation products		Remarks	Reference
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Field soil dissipation and accumulation: The "TNsG" states that field soil dissipation and accumulation are required in two soil types if a. The $DT_{90field}$ is over one year and; b. The $DT_{50field}$ is greater than 3 months or; c. If during laboratory tests non-extractable residues are formed in amounts exceeding 70% of the initial dose after 100 days with a mineralization rate of less than 5% in 100 days. Silicon dioxide has the molecular formula O=Si=O and the approved test guideline OECD 304A applies only to ^{14}C-labelled material. Notwithstanding the above, the preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment, and therefore it is not considered necessary to submit additional data on field soil dissipation and accumulation. Therefore an initial aerobic degradation study in soil has not been submitted.	Document IIIA Section 7.2.2.2
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Extent and nature of bound residues: The "TNsG" states that data on the extent and nature of bound residues on soil are required if data submitted in Document IIIA, Section A7.2.1 and A7.2.2.1 indicate that bound residues may be formed which account for more than 10% of the active substance added. This end point is not relevant for silicon dioxide, on the basis on data submitted in Document IIIA, Section A7.2.1 and A7.2.2.1.	Document IIIA Section 7.2.2.3

Absorption onto/desorption from soils (4 of 4)

Guideline/ test method	Absorbed a.s. [%]	K_a [1]	K_{aOC} [2]	K_d [3]	K_{dOC} [4]	K_a / K_d [5]	Degradation products		Remarks	Reference
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Other soil degradation studies: The preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment, and therefore it is not considered necessary to submit additional data on release to soil under different release conditions.	Document IIIA Section 7.2.2.4
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Adsorption and mobility in soil further studies: The preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment, and therefore it is not considered necessary to submit additional data on adsorption and mobility studies in soil.	Document IIIA Section 7.2.3
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Adsorption and desorption in accordance with the new test guideline EC C18 or the corresponding OECD 106 and, where relevant, adsorption and desorption metabolites and degradation products: Silicon dioxide, under normal conditions of use in Rentokil Initial's insecticide (PT18) products, will not be applied directly on soil or released to soil in relevant concentrations. The preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment, and therefore it is not considered necessary to submit additional data on adsorption and mobility studies in soil.	Document IIIA Section 7.2.3.1
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Mobility in at least three soil types and where relevant mobility of metabolites and degradation products: The preliminary risk assessment for exposure to soil does not indicate the need to conduct studies on the fate and behaviour of silicon dioxide in the soil compartment, and therefore it is not considered necessary to submit additional data on mobility of silicon dioxide in soil.	Document IIIA Section 7.2.3.2

Key

1. K_a = Adsorption coefficient.
2. K_{aOC} = Adsorption coefficient based on organic carbon content.
3. K_d = Desorption coefficient.
4. K_{dOC} = Desorption coefficient based on organic carbon content.
5. K_a/K_d = Adsorption/desorption distribution coefficient.

4.1.2 Accumulation

Measurements of aquatic bioconcentration

Guideline /Test method	Exposure	Log Pow of a.s.	Initial concentration of a.s.	Steady-state BCF	Uptake rate constant	Depuration rate constant	Depuration time (DT_{50})	Metabolites	Remarks	Reference
N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	"Bioconcentration" is the process leading to a higher concentration of, for example, a pesticide in an organism than in environmental media to which it is exposed. The "Technical Guidance Document in support of Commission Directive 93.67/EEC on risk assessment for new notified substances and Commission Regulation EC No 1488/94 on risk assessment for existing substances. Part II Environmental risk assessment" states that the following are indicators of bioaccumulation potential a. if the substance has a partition coefficient log Kow ≥ 3 or; b. the substance is highly adsorptive or; c. the substance belongs to a class of substances known to have a potential to accumulate in living organisms or; d. there are indications from structural features. From the data available, silicon dioxide is not expected to have an intrinsic potential for bioconcentration in aquatic organisms, on the basis that it has an estimated partition coefficient of 0.53 (refer to Document IIIA, Section 3.9 for detail).	Document IIIA Section 7.4.2

Estimations on aquatic bioconcentration

Basis for estimation	Log Pow (measured)	Estimated BCF for fish (freshwater)	Estimated BCF for fish eating bird/predator	Remarks	Reference
N/A	N/A	N/A	N/A	"Bioconcentration" is the process leading to a higher concentration of, for example, a pesticide in an organism than in environmental media to which it is exposed. The "Technical Guidance Document in support of Commission Directive 93.67/EEC on risk assessment for new notified substances and Commission Regulation EC No 1488/94 on risk assessment for existing substances. Part II Environmental risk assessment" states that the following are indicators of bioaccumulation potential a. if the substance has a partition coefficient log Kow ≥ 3 or; b. the substance is highly adsorptive or; c. the substance belongs to a class of substances known to have a potential to accumulate in living organisms or; d. there are indications from structural features. From the data available, silicon dioxide is not expected to have an intrinsic potential for bioconcentration in aquatic organisms, on the basis that it has an estimated partition coefficient of 0.53 (refer to Document IIIA, Section 3.9 for detail).	Document IIIA Section 7.4.2

Estimation on terrestrial bioconcentration

Basis for estimation	Log Pow (measured)	Estimated BCF for				Remarks	Reference
		Terrestrial food chain I		Terrestrial food chain II			
		Soil dwelling species	Predatory bird/ vertebrate	Terrestrial plant	Grazing non-target organism		
N/A	N/A	N/A	N/A	N/A	N/A	"Bioconcentration" is the process leading to a higher concentration of, for example, a pesticide in an organism than in environmental media to which it is exposed. The "Technical Guidance Document in support of Commission Directive 93.67/EEC on risk assessment for new notified substances and Commission Regulation EC No 1488/94 on risk assessment for existing substances. Part II Environmental risk assessment" states that the following are indicators of bioaccumulation potential a. if the substance has a partition coefficient log Kow ≥ 3 or; b. the substance is highly adsorptive or; c. the substance belongs to a class of substances known to have a potential to accumulate in living organisms or; d. there are indications from structural features. From the data available, silicon dioxide is not expected to have an intrinsic potential for bioconcentration in aquatic organisms, on the basis that it has an estimated partition coefficient of 0.53 (refer to Document IIIA, Section 3.9 for detail).	Document IIIA Section 7.5.5

Footnote
The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products" states that a test on bioconcentration in earthworms is required if the risk assessment for secondary poisoning would suggest a concern for predators (Document IIA, Section 7.5.5.1). The environmental risk assessment for silicon dioxide shows there is no risk of secondary poisoning under normal conditions of use in Rentokil Initial's insecticide (PT 18) products. As there is no concern for predators, the test to determine bioconcentration of silicon dioxide in earthworms is not considered necessary.

4.2 EFFECT ON ENVIRONMENTAL ORGANISMS

4.2.1 Aquatic compartment

Acute toxicity to fish

Guideline/ Test method	Species	Endpoint/ Type of test	Exposure Design	Duration	Results LC_0 LC_{50} LC_{100}	Remarks	Reference
OECD Guidelines for Testing of Chemicals. Method 203. Fish, Acute Toxicity Test. Adopted 17 July 1992.	*Oncorhynchus mykiss*	Acute toxicity	The test procedure employed was a static system. Single borosilicate glass vessels (external dimensions; 460 mm × 305 mm × 310 mm; length × width × height) were used for the dilution water control and the exposure solution. The vessels had a working volume of 25 L. The test was undertaken in a temperature controlled room which was set at the nominal test temperature of 15 ± 1°C. The test solutions were gently aerated. The photoperiod in this study was 16 hours fluorescent light and 8 hours dark with 20 minute dawn and dusk transition periods commencing at 06:00 and 21:40 hours. At the start of the test ten fish were randomly allocated to the single test concentration and the dilution water control. The fish were not fed during the course of the test.	96 h	NOEC = 110 mg/L	There were no mortalities at the limit of solubility for amorphous silicon dioxide.	Document IIIA, Section 7.4.1.1

Footnotes

1. Due to the results available on the acute toxicity of silicon dioxide to fish, coupled with the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide to aquatic organisms (the data requirements detailed in Document IIIA, Section 7.4.3). It is also not necessary to submit data on prolonged toxicity of silicon dioxide to fish (Document IIIA, Section 7.4.3.1).

2. Due to the results available in the core base set of environmental toxicity data for silicon dioxide, particularly the lack of acute toxicity to fish and the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide on the reproduction and growth rate of fish (the data requirements detailed in Document IIIA, Section 7.4.3.2).

3. Due to the fact that there is no exposure to the aquatic environment, coupled with the fact that there is no data available which suggests that silicon dioxide will bioaccumulate in the environment, nor is there a risk of secondary poisoning through the use of silicon dioxide, it is not necessary to submit data on bioaccumulation in fish (the data requirements detailed in Document IIIA, Section 7.4.3.3.1).

Acute toxicity to invertebrates

Guideline/ Test method	Endpoint / Type of test	Exposure Design	Duration	Results LC_0 LC_{50} LC_{100}	Remarks	Reference
OECD Guidelines for the Testing of Chemicals. Test Guideline 202 Part I, Daphnia sp., Acute Immobilisation Test. Adopted 4 April 1984.	Acute toxicity	Borosilicate glass beakers of 250 ml nominal capacity were used as test vessels, with four replicates for the dilution water control and exposure solution. Each vessel contained 200 ml of test solution providing a depth of approximately 60 mm. The beakers were covered with loose fitting glass lids. The positions of the treatments were randomly allocated within the test area. The test was initiated by the addition of five randomly selected *Daphnia*, in <2.0 ml of dilution water, to each test vessel. The dilution water control and exposure solution contained a total of 20 *Daphnia*. The loading of the *Daphnia* in each test vessel was 25 *Daphnia*/L. The nominal test solution temperature was 20 ± 1°C, maintained by control of the room temperature. A photoperiod of 16 hours light:8 hours dark, with 20 minute dusk and dawn transition periods, was provided. The test solutions were not aerated and the *Daphnia* were not fed during the course of the study.	48 h	NOEC = 86 mg/L	No symptoms of toxicity were observed in this study.	Document IIIA, Section 7.4.1.2

Footnotes

1. Due to the results available on the acute toxicity of silicon dioxide to *Daphnia magna*, coupled with the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide to aquatic organisms (the data requirements detailed in Document IIIA, Section 7.4.3).

2. Due to the fact that there is no exposure to the aquatic environment, coupled with the fact that there is no data available which suggests that silicon dioxide will bioaccumulate in the environment, nor is there a risk of secondary poisoning through the use of silicon dioxide, it is not necessary to submit data on bioaccumulation in invertebrate species (the data requirements detailed in Document IIIA, Section 7.4.3.3.2).

3. Due to the results available in the core base set of environmental toxicity data for silicon dioxide, particularly that available on the acute toxicity to *Daphnia magna* and the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide on the reproduction and growth rate of invertebrates (the data requirements detailed in Document IIIA, Section 7.4.3.4).

Growth inhibition on algae

Guideline / Test method	Species	Endpoint / Type of test	Exposure		Results			Remarks	Reference
			Design	Duration	NOE_rC	E_bC_{50} [1]	E_rC_{50} [2]		
OECD Guidelines for Testing of Chemicals. Test Guideline 201. Alga, Growth Inhibition Test. Adopted 7 June 1984.	*Selenatrum capricornutum*	Growth inhibition test	The test vessels were borosilicate glass conical flasks of 250 ml nominal capacity closed with polyurethane foam bungs. Each flask contained 100 ml of test solution. The cultures were incubated at 24 ± 2°C (the nominal test temperature), under continuous "cool-white" illumination, with orbital shaking at 160 rpm, in a Gallenkamp type INR-401 orbital incubator. Six replicate cultures of the culture medium control and single concentration of test substance were employed. The positions of the test vessels in the incubator were randomised by rows, and re-randomised daily. One blank vessel (without algal inoculum) for the culture medium control and each test concentration was incubated concurrently. The algal cell densities of the inoculum and test cultures were determined by electronic particle counting, using a Coulter counter model Z1, counting at a lower threshold equivalent spherical diameter of approximately 2.3 µm. Each replicate test vessel was inoculated with 0.79 ml of the inoculum culture to give a nominal cell density of 1.00×10^4 cells/mL. Three 100 ml volumes of Coulter electrolyte, inoculated in the same manner, had a mean measured cell density of 1.01×10^4 cells/mL. The latter value was used for growth calculations. After 24, 48 and 72 hours, (1, 2 and 3 days) samples were removed from each test and blank vessel. The appropriate blank particle count was subtracted from that of the test culture to obtain the cell density.	72 h	54 mg/L	> 54 mg/L	> 54 mg/L	No inhibition was observed.	Document IIIA, Section 7.4.1.3

Key

1. Calculated from the area under the growth curve
2. Calculated from growth rate

Footnotes

1. Due to the results available on the toxicity of silicon dioxide to algae, coupled with the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide to aquatic organisms (the data requirements detailed in Document IIIA, Section 7.4.3).

Inhibition of microbial activity (aquatic)

Guideline / Test method	Species / Inoculum	Endpoint/ Type of test	Exposure		Results			Remarks	Reference
			Design	Duration	EC_{20}	EC_{50}	EC_{80}		
OECD Test Guideline 209, Activated Sludge, Respiration Inhibition Test. Adopted 4 April 1984.	Activated sludge from [redacted] treating sewage of predominantly domestic origin.	Respiration inhibition	This test measures the respiration rate of an activated sludge 3 hours after feeding an excess, but standard amount, of a synthetic sewage and compares this with the respiration rate of the same activated sludge in the presence of the test chemical. 3,5-dichlorophenol is used as a reference substance as it has known inhibitory effects on respiration and ensures that the batch of sludge used in the test shows a normal level of sensitivity. A single nominal 1000 mg/L concentration of test substance was prepared in duplicate together with three control culture flasks. Four flasks containing the reference substance, 3,5-dichlorophenol, at nominal concentrations of 3.2, 10, 32 and 100 mg/L were also prepared. In addition a single abiotic flask containing 100 mg/L 3,5-dichlorophenol but no activated sludge was prepared. Each flask contained an excess of the synthetic sewage, sufficient activated sludge to give final solids concentrations of 1600 mg/L, an appropriate quantity of either test substance or 3,5-dichlorophenol stock solution and aerated water to give a final flask contents volume of 500 ml. The exact quantities of each of these constituents are given in Table A7_4_1_4-5. The pH of each flask was measured before the start of the test. Flasks were set up in batches of six and aerated at 20 ± 2°C for 3 hours. Each batch included a control flask and five test or reference substance flasks. The temperatures of the flask contents were measured at the end of the 3 hours aeration using a mercury-in-glass thermometer.	3 h	>1000 mg/L	>1000 mg/L	>1000 mg/L	No inhibition occurred due to application of the test material. NOEC = 1000 mg/L	Document IIIA, Section 7.4.1.4

Footnotes

1. Due to the results available on the toxicity of silicon dioxide to microbes, coupled with the fact that there is no exposure to the aquatic environment, it is not necessary to submit further studies on the effects of silicon dioxide to aquatic organisms (the data requirements detailed in Document IIIA, Section 7.4.3).

Effects on sediment dwelling organisms

Remarks	Reference
The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products" states that this information is only required if the active substance partitions to, and persists in, aquatic sediments such that sediment dwelling organisms are likely to be exposed to the active substance. The core base data set for silicon dioxide does not indicate that silicon dioxide poses a danger to sediment dwelling organisms. In addition, the environmental risk assessment for silicon dioxide shows that no exposure of sediment dwelling organisms is expected under normal conditions of use in Rentokil Initial's insecticide (PT18) products. It is for these reasons that a study to determine the effects of silicon dioxide on sediment dwelling organisms has not been submitted.	Document IIIA, Section 7.4.3.5.1

Aquatic Plant Toxicity

Remarks	Reference
The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products" states that further studies on the effects on aquatic organisms, such as aquatic plants, are required only if the results of data submitted for the end points in Document IIIA, Sections 7.4.1.1, 7.4.1.2, 7.4.1.3 and 7.4.1.4 indicate a danger to the environment. As the results of the tests submitted for the end points in Document IIIA, Sections 7.4.1.1, 7.4.1.2, 7.4.1.3 and 7.4.1.4 do not indicate that silicon dioxide poses a danger to the environment, it is not considered necessary to submit data that considers toxicity of silicon dioxide to aquatic plants.	Document IIIA, Section 7.4.3.5.2

4.2.2 Atmosphere

Silicon dioxide is not volatile, and therefore exposure via the atmospheric compartment is not considered relevant.
Notwithstanding the above, the structure of silicon dioxide is O=Si=O. This structure means that OH-radicals are unlikely to be generated during degradation in air. When pseudo-first order rate constant for degradation in air was estimated using the QSAR method, the rate constant was zero. This result supports the above statement that OH radicals are unlikely to be generated during degradation of silicon dioxide in air.
Silicon dioxide will not have an impact on global warming because it does not exist in the gaseous state at ambient temperature and pressure. The presence of absorption bands in the IR spectrum region 800-1200nm is therefore not applicable. It is also highly unlikely that silicon dioxide will have any impact either on ozone depletion in the stratosphere or ozone formation in the troposphere. This is because silicon dioxide does not contain chlorine substituents, and OH radicals are unlikely to be generated during degradation of silicon dioxide in air. The final atmospheric risk indicator is acidification. As silicon dioxide does not contain Cl, F, N or S substituents, acidification is not considered to be a risk to receiving soil or surface water.

4.2.3 Terrestrial compartment

Toxicity to terrestrial organisms, initial tests (1 of 2)

Guideline /Test method	Species	Endpoint / Type of test	Exposure Design	Exposure Duration	Results NOEC	Results LOEC	Results EC/ LC_{50}	Remarks	Reference
N/A	Microbes, terrestrial	Inhibition	N/A	N/A	N/A	N/A	N/A	The environmental risk assessment for silicon dioxide does not indicate that it poses a risk to the terrestrial compartment. Therefore it is not considered necessary to submit data on the effect of silicon dioxide on the inhibition of microbial activity in the terrestrial compartment.	Document IIIA, Section 7.5.1.1
N/A	Earthworm	Acute toxicity	N/A	N/A	N/A	N/A	N/A	The information on the environmental exposure scenario for silicon dioxide (as given in Document IIIB, Section 7.1) does not indicate that it poses a risk to the terrestrial compartment. Therefore it is not considered necessary to submit data on the acute toxicity of silicon dioxide to earthworms.	Document IIIA, Section 7.5.1.2
N/A	Plants	Acute toxicity	N/A	N/A	N/A	N/A	N/A	The environmental risk assessment for silicon dioxide does not indicate that it poses a risk to the terrestrial compartment. It is on this basis that it is not considered necessary to submit data on the acute toxicity of silicon dioxide to plants.	Document IIIA, Section 7.5.1.3
N/A	Birds	Acute oral Short term Reproduction	N/A	N/A	N/A	N/A	N/A	Silicon dioxide, under normal conditions of use in Rentokil Initial's insecticide (PT 18) products will be applied indoors only. Data submitted in Document IIIA, section 7.4.2 shows that silicon dioxide is not expected to have an intrinsic potential for bioaccumulation. The environmental risk assessment for silicon dioxide shows there is no risk of secondary poisoning under normal conditions of use in Rentokil Initial's insecticide (PT 18) products. There is no data available to suggest that silicon dioxide is hazardous to birds. Therefore studies determining the acute oral toxicity, short term toxicity and effects on reproduction of silicon dioxide to birds have not been submitted.	Document IIIA, Sections 7.5.3.1.1 7.5.3.1.2 7.5.3.1.3
N/A	Honeybee and other beneficial arthropods	Acute toxicity	N/A	N/A	N/A	N/A	N/A	As silicon dioxide, under normal conditions of use in Rentokil Initial's insecticide (PT 18) products will be applied indoors only, it is not considered necessary to conduct this test.	Document IIIA, Section 7.5.4.1

Toxicity to terrestrial organisms, initial tests (2 of 2)

Guideline /Test method	Species	Endpoint / Type of test	Exposure Design	Exposure Duration	Results NOEC	Results LOEC	Results EC/ LC_{50}	Remarks	Reference
N/A	Other terrestrial non-target organism	N/A	N/A	N/A	N/A	N/A	N/A	The environmental risk assessment for silicon dioxide does not indicate that it poses a risk to the terrestrial compartment, or is there long-term exposure. Therefore it is not considered necessary to submit data to determine the effects of silicon dioxide on other terrestrial non-target organisms.	Document IIIA, Section 7.5.6
N/A	Mammals	N/A	N/A	N/A	N/A	N/A	N/A	The environmental risk assessment for silicon dioxide does not indicate that it poses a risk to the terrestrial environment. The toxicity profile of silicon dioxide as shown in Document IIIA, Section 6 Toxicological and Metabolic Studies does not indicate a concern regarding toxicity to mammals. It is for these reasons that it is not considered necessary to determine the effect of increased silicon dioxide exposure to mammals. Given the above justification, it is not necessary to submit data to meet the following data end points: 7.5.7.1.1 Acute oral toxicity (mammals) 7.5.7.1.2 Short term toxicity (mammals) 7.5.7.1.3 Effects on reproduction (mammals) Note that these points have been addressed for silicon dioxide in Document IIIA, Section 6 Toxicological and Metabolic Studies. Further studies are not required.	Document IIIA, Section 7.5.7.1.1 Document IIIA, Section 7.5.7.1.2 Document IIIA, Section 7.5.7.1.3

Footnotes

1. Due to the results available in the core base set of environmental toxicity data for silicon dioxide, particularly that available on the toxicity to earthworms and the fact that there is no exposure to the terrestrial environment, it is not necessary to submit further studies on the effects of silicon dioxide on the reproduction of earthworms or other soil non-target macro-organisms (the data requirements detailed in Document IIIA, Section 7.5.2.1).

2. Due to the results available in the core base set of environmental toxicity data for silicon dioxide, particularly that available on the toxicity to plants and the fact that there is no exposure to the terrestrial environment, it is not necessary to submit further studies on the long term effects of silicon dioxide on plants (the data requirements detailed in Document IIIA, Section 7.5.2.2).

4.2.4 Non compartment specific effects relevant to the food chain (secondary poisoning)

Result
The assessment of the potential impact of substances on top predators is based on the accumulation of hydrophobic chemicals through the food chains. Ideally a comparison between concentrations found in top predators should be made with the no effect concentration for that predator. As this data is not available a theoretical assessment is made. The first step in the assessment is to consider bioaccumulation potential. This has been assessed as unlikely to occur. Next the classification on the basis of mammalian toxicity is considered. Amorphous silicon dioxide is not classified as dangerous therefore it is not in the list of classifications to cause concern (i.e. R48, R60, R61, R62, R63, or R64.) In addition there is no indication of genotoxicity, although not directly relevant for the environment it may be indicative for top predators. Because amorphous silicon dioxide is not classified in the categories above and because there are no other indications, such as endocrine disruption, it is not necessary to perform an assessment of secondary poisoning. (Technical Guidance Document on Risk Assessment Part II Chapter 3 Section 3.8.3.1 (2003)).

Section A8.1
Annex Point IIA, VIII, 8.1

Recommended Methods and Precautions concerning Handling, Use, Storage, Transport or Fire.

Official use only

1. REFERENCE

1.1 References

[redacted]

1.2 Details

Handling:	Avoid generation of dust. A considerable static electrical charge can be built up during mechanical handling which may become a hazard in atmospheres containing flammable vapours.
Use:	Avoid inhalation of dusts. Wherever possible use engineering controls to prevent or control operator exposure. Such engineering control methods include process or personal enclosure, mechanical ventilation (dilution and local exhaust) and control of process conditions. Wear suitable protective equipment if working in confined spaces with inadequate ventilation, or where there is any risk of the occupational exposure limits being exceeded. Wear suitable protective clothing, coveralls and plastic or rubber gloves. Also wear suitable eye protection such as goggles or safety spectacles. Do not eat, drink or smoke in the workplace and wear protective equipment to comply with good occupational hygiene practice.
Storage:	Store in original container. Keep container tightly closed, and dry.
Conditions to Avoid:	None known. However, note that silicon dioxide is hygroscopic.
Materials to Avoid:	None known.
Hazardous Breakdown Products:	None known.
Transport:	Silicon dioxide is not classified as hazardous for transport.
Fire:	Not applicable. Silicon dioxide is a non-combustible powder.
Accidental Release:	Contain spillages. Dampening with water can reduce dust. Sweep or preferably vacuum up and collect in suitable containers for re-use or disposal.

Section A8.2 **In case of fire, nature of reaction products, combustion gases, etc.**
Annex Point IIA, VIII, 8.2

Official use only

1. **REFERENCE**

1.1 Reference [redacted]

1.2 Details Silicon dioxide is a non-combustible powder. No hazardous breakdown products or other reaction products are known for silicon dioxide, in case of fire.

Section A8.3
Annex Point IIA, VIII, 8.3

Emergency Measures in case of an accident

Official use only

1. REFERENCE

1.1 Reference

[redacted]

1.2 Details

First Aid Advice:

Inhalation: Remove patient to fresh air, keep warm and at rest If symptoms develop, obtain medical attention.

Eye contact: If substance has got into eyes, immediately wash out with plenty of water. Obtain immediate medical attention.

Skin contact: Wash affected skin with plenty of water. If symptoms develop, obtain medical attention.

Ingestion: Do not induce vomiting. Wash out mouth with water. If large amount swallowed or symptoms develop, seek medical attention.

Accidental Release:

Contain spillages. Dampening with water can reduce dust. Sweep or preferably vacuum up and collect in suitable containers for re-use or disposal.

Section A8.4
Annex Point IIA, VIII, 8.4

Possibility of destruction or decontamination following release in or on the following: (a) Air, (b) Water, including drinking water, and (c) Soil.

Official use only

1. REFERENCE

1.1 Reference

[redacted]

1.2 Details

Do NOT contaminate watercourses or ground.

Notwithstanding the above, amorphous silicon dioxide is virtually inert and has no known adverse effect on the environment. If large amounts of silicon dioxide are accidentally released, contain spillage. Dampening with water can reduce dust. Sweep or preferably vacuum up and collect in suitable containers for re-use or disposal.

Section A8.5
Annex Point IIA, VIII, 8.5

Procedures for waste management of the active substance for industry or professional users.

Official use only

1. Details

Silicon dioxide is not classified as hazardous waste according to Council Directive 91/689/EC, Commission Decision 2000/532/EC (Amended), Commission Decision 2001/118/EC.

Empty containers of silicon dioxide are not re-used or recycled. Empty containers of silicon dioxide are not cleaned prior to disposal (e.g. rinsed). Empty containers are disposed of either to landfill. No pre-treatment of the empty containers are necessary prior to disposal.

Waste powder (either in normal use or quantities involved in spills) can be collected up and re-used (if considered appropriate), otherwise it is disposed of. Disposal of waste powder is to landfill. No pre-treatment of the waste powder is necessary prior to disposal.

Note that silicon dioxide is not used in treated products or treated materials, nor is it applied to a system with water. Therefore no information has been provided regarding disposal of waste generated from these uses.

Section A8.5.1 Possibility of re-use or recycling

Annex Point IIA, VIII, 8.5.1

			Official use only
1.	**Details**	Wherever possible, spilt material, once collected is re-used but re-use of this material would be considered on a case-by-case basis.	

Section A8.5.2 Possibility of neutralisation of effects

Annex Point IIA, VIII, 8.5.2

Official use only

1.	**Details**	Neutralisation procedures for silicon dioxide are not considered necessary given that synthetic amorphous silicon dioxide is virtually inert and has no hazardous decomposition or reaction products. The procedure for dealing with both a small and large spillage of silicon dioxide is described in section A8.3 and section A8.4.

Section A8.5.3
Annex Point IIA, VIII, 8.5.3

Conditions of controlled discharge including leachate qualities on disposal.

Official use only

1. Details

Disposal should be accordance with local, state or national legislation. Silicon dioxide is not classified as hazardous waste under EC Directive 91/689/EEC and therefore may be disposed of by landfill in accordance with local regulations. As silicon dioxide is essentially inert and insoluble in water, no preliminary treatments are necessary before controlled landfill.

Any waste material from the manufacture of amorphous silicon dioxide for use as an insecticide (PT18) is sent to landfill in sealed containers.

The possible routes of exposure to the environment are *via* leachate from landfill entering a sewage treatment plant then from there in sludge and into treated water. However, the risk to the environment from the act of disposal is considered to be insignificant. This is because the quantity of amorphous silicon dioxide being disposed of, compared to the volume of total waste is minute. The total estimated use of amorphous silicon dioxide across the whole of the EU is < 0.00000073% of the total waste generated and sent to landfill in the UK alone*. This means that any amorphous silicon dioxide that is sent for landfill is massively diluted by the large volume of municipal waste continually entering landfill sites in the UK. The data available on the environmental toxicity of amorphous silicon dioxide (as given in Document IIIA, Section 7) shows that this volume will not cause any adverse effect to the environment, and as such requires no further investigation.

*Refer to Document IIIB Section 7.1 for more details of the scientific reasoning that supports this statement.

Section A8.5.4 **Conditions for controlled incineration.**

Annex Point IIA, VIII, 8.5.4

Official use only

1.	**Details**	Controlled incineration is not a specified method of waste disposal for silicon dioxide. Notwithstanding the fact that silicon dioxide is a non-combustible powder, because silicon dioxide is not hazardous according to EC Directive 91/689/EEC and it is essentially inert, it may be disposed of by landfill according to local regulations. As controlled incineration is not a specified method of waste disposal for silicon dioxide it is not necessary to provide information on the conditions needed for it's safe incineration.

Section A8.6
Annex Point IIA, VIII 8.6

Observations on undesirable or unintended side-effects, for example, on beneficial and other non-target organisms

Official use only

1. Details

The mode of action of silicon dioxide is unlike conventional active ingredients (e.g. neurotoxins or chemical growth regulators). Silicon dioxide absorbs waxes from the insect's cuticle (the thin, waxy protective outer layer which prevents dehydration in dry atmospheres). The loss of these waxes initiates a rapid loss of water from the insect's body, which leads to death by desiccation[1].

Given the mode of action, and the fact that silicon dioxide is an approved food additive*, there is no risk to non-target vertebrates and humans.

The potential for adverse effects on non-target insects from the use of silicon dioxide in insecticide products is minimised from restrictions on their use, for example RID Insect Powder is intended for use indoors only. Measures such as these minimise the risk of secondary poisoning of non-target insects and invertebrate wildlife.

Given the above, it is concluded that there will be no undesirable or unintended side effects for beneficial and other non-target insects through the use of silicon dioxide as a biocide.

*Silicon dioxide is an approved food additive[2], assigned the E number E551[3], and is used as an anti-caking agent. Silicon dioxide has been given an acceptable daily intake of "not limited".

References

[redacted]

Section A8.7
Annex Point IIIA, VIII, 8.7

Identification of any substances falling within scope of List I or List II of the Annex to Directive 80/68/EEC on the protection of ground water against pollution caused by certain dangerous substances.

Official use only

1. Details

Silicon dioxide is listed in List II of the Annex to Directive 80/68/EC (OJ No. L20, 26/1/1980, p. 43).

None of the impurities present in silicon dioxide are listed in either List I or II of the Annex to Directive 80/68/EC (OJ No. L20, 26/1/1980, p. 43).

Section A9 **Classification and Labelling**
Annex Point IIAIX

Official use only

1. Details

Classification: Non-hazardous according to EC Directive 67/548/EEC.
Silicon dioxide is not listed in Annex I of Directive 67/548/EEC and there is no data available to suggest it is hazardous to health or the environment. It is on this basis that silicon dioxide has been classified as non-hazardous.

Labelling:

Category of danger:	Not required.
Risk Phrases:	Not required.
Safety Phrases:	Not required.

Note that the following information is identical to that found in Document IIA

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS- No.	112926-00-8
EINECS-No.	231-545-4
Other-No. (CIPAC, ELINCS)	None known.
IUPAC Name	Silicon dioxide
Common name, synonyms	Silica
Molecular formula	SiO2
Structural formula	O=[Si]=O
Molecular weight (g/mol)	60.08 g/mol

1.2 PURITY/IMPURITIES, ADDITIVES

Purity: [redacted] silicon dioxide.

[redacted]

[redacted]

Additives:

[redacted]

[redacted]

[redacted]

1.3 PHYSICO-CHEMICAL PROPERTIES

Melting point	1710°C
Boiling point	Ca. 2230°C
Density	Tap density: 0.13 g/mL
Vapour pressure	Not applicable, as melting point is above 300°C
Henry's Law Constant	Not applicable, figure can not be calculated as vapour pressure has not been determined.
Appearance	Physical state : Solid (powder) at 20°C, 101.3 kPa. Colour: White at 20°C, 101.3 kPa. Odour: Odourless at 20°C, 101.3 kPa.
Absorption Spectra	
Mass Spectrum	
Solubility in water	112.739 mg/L
Dissociation constant	Not applicable, as solubility has been meaured.
Solubility in organic solvents	Insoluble.
Stability in organic solvents	Not applicable, as no organic solvents are used in the manufacture of the active substance.
Partition coefficient (n-octanol/water)	n-octanol / water: log pow 0.53 (calculated)
Surface tension	57.5 dynes/cm
Viscosity	Not applicable, as silicon dioxide is a solid.

1.4 ANALYTICAL METHOD FOR DETECTION AND IDENTIFICATION

1.4.1 Analysis of active substance as manufactured

Sample	Test substance	Analytical method	Fortification range/Number of measurements	Linearity	Specificity	Recovery rate (%)			Limit of determination	Reference
						Range	Mean	St. dev.		
Gasil 23D	Amorphous silicon dioxide	ICP-AES	3	$r^2 = \geq 0.995$	There are no significant interferences affecting the instrumental response for silicon.	99.3-104% for 3 replicates at 1, 5 and 50 ppm	99.6, 99.7, 103 for 3 replicates	Not reported.	0.03 ppm	Document IIIA, Section 4.1

[redacted]

1.4.2 Formulation analysis

A method has been provided for analysis of the active ingredient, amorphous silicon dioxide, [redacted], in the formulated product, RID Insect Powder. See Document IIIB, Section 4.1 for RID Insect Powder analysis.

1.4.3 Residue analysis

Residue analysis for the active ingredient in soil
ISO method 14869-2:2002(E) used to extract silicon from soil can be used in combination with ICP-AES detection to analyse the amount of silicon dioxide the sample then through back calculation silicon dioxide content can be examined. See document IIIA, Section 4.2 (a) for further details.

Residue analysis for the active ingredient in air
Method of analysis used is NIOSH, 1994, NIOSH Manual of Analytical Methods (NMAM), Fourth Edition SILICA, AMORPHOUS Method 7501, Issue 2. See document IIIA, Section 4.2 (b) for further details.

Residue analysis for the active ingredient in water
Methods of analysis have been developed based on ICP-AES in the following media: Drinking water, ground water and surface water. See documents IIIA, Sections 4.2 (c) to (g) for further details.

Animal and human body fluids and tissues
As silicon dioxide is not classified as hazardous for supply, it is not necessary to provide an analytical method for detection in body fluids and tissues according to the "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products".

Residue analysis for the active ingredient in food, feeding stuffs and other products
Not applicable. Residue analysis is required only if the product and/or active ingredient is intended for use where food for human consumption or feed for livestock is prepared, consumed or stored. Neither silicon dioxide (or the representative product RID Insect Powder) is intended for use where food for human consumption or feed for livestock is prepared, consumed or stored.

1.5 CLASSIFICATION AND LABELLING

1.5.1 Current classification

Current classification of a.s.

Classification	Non-hazardous according to EC Directive 67/548/EEC
Class of danger	Not required.
R phrases	Not required.
S phrases	Not required.

1.5.2 Proposed classification

Not applicable. Silicon dioxide will be classified according to EC Directive 67/548/EEC (as detailed in 1.5.1).

2. EFFECTIVENESS AGAINST TARGET ORGANISMS

2.1 FUNCTION

Insecticide for the control of cockroaches, such as the oriental cockroach, *Blatta orientalis;* the German cockroach, *Blatella germanica.*

2.2 FIELD OF USE ENVISAGED

MG03: Pest Control.
Product type 18.
For professional users only.

2.3 EFFECTS ON TARGET ORGANISMS

Experimental data on the effectiveness of the active substance against target organisms

Test substance	Test organism(s)	Test system/ concentrations applied/exposure time	Test results: Effects, mode of action, resistance	Reference
Silicon dioxide (specification identical to that given in section 2 of application)	Laboratory culture of the oriental cockroach *Blatta orientalis*. In this experiment, *Blatta orientalis*. oothecae, were allowed to hatch onto silica dust.	Exposure in polystyrene pots: 20 Oothecae no more than one day old were placed singly in polystyrene pots containing 0.01g silica dust. Pots of dust had been equilibrated for at least 24h under test conditions. Number of nymphs and date of hatch were recorded. Survival of nymphs was recorded one and two days after hatching. Non-hatching oothecae were retained in the test pots for between 84 and 89 days before discarding. Control without dust were used. Exposure in petri dishes: 0.01g silica dust was spread evenly over filter paper in the base of a clear polystyrene petri dish. In the centre of the treated paper was placed a 2 x 2cm square of untreated filter paper. Five oothecae were placed on this untreated filter paper. Oothecae were inspected for hatching every half an hour. As soon as the nymphs had hatched in any of the dishes, all the oothecae including the hatched one and the square of untreated filter paper were removed from the dish, forcing the nymphs into contact with the silica dust. Hatched nymphs were observed half-hourly for a further three hours for mortality. A total of 50 oothecae were observed.	Exposure in polystyrene pots There were no significant differences between exposed and unexposed controls with respect to numbers or ages of oothecae on hatching. One day after any particular batch of emerging nymphs was first seen, all were dead. It is concluded that exposure to silica dust does not effect the viability of cockroach oothecae, however nymphs hatching into dust are all dead within one day of first being recorded. Exposure in petri dishes Exposure to silica dust produced 100% mortality of newly hatched cockroach nymphs in less than 2.5h. It was noted, in this experiment, that as soon as the nymphs hatched they moved readily from the untreated filter paper onto the silica dust without encouragement. This indicates that the dusts are not excessively repellent to nymphs. It is concluded that exposure to silica dust does not effect the viability of cockroach oothecae, however nymphs hatching into dust are all dead within 3 hours. Results do not give an indication about development of resistance or mode of action. See footnote.	Document IIIA, Section 5.3.1.
Silicon dioxide (specification identical to that given in section 2 of application)	Laboratory culture of the oriental cockroach *Blatta orientalis*. 10 adult *Blatta orientalis*. Cockroaches (5 male and 5 female) were used.	Cockroaches (5 male and 5 female) were exposed to silica dust in 4 choice chambers. The aim of the test was to establish efficacy of the dust, but also to establish, by observing the insects, whether the dust was repellent. The foil-lined floor of each chamber was covered by filter paper to provide a standardised textured surface on which cockroaches could walk without slipping. Each chamber was divided into halves by a strip of wood to restrict the spreading of dust by cockroaches from the treated to the untreated half of the chambers. Immediately prior to each experimental run, an evenly distributed deposit of 0.5g of silica dust (= 3.4g/m^2) was applied to the floor of one half of the choice chamber. In some repetitions, silica dust was applied at a nominal dosage of 1.1 g/m^2. The insects were held in the choice chambers for 72h during which their positions were noted. Times of death were also noted.	Mortality of adult *Blatta orientalis* cockroaches were 90-100% after 72h exposure without water; 20-60% with water. It was noted that cockroaches have a tendency to spend less time in the treated side of the chamber if water is unavailable. Despite a greater proportion of time spent in the treated side, mortality was less when water was available. Apparently, ingestion of water and/or slightly elevated humidity in chambers with water available more than compensated for increased exposure to dusts. It was noted during this experiment that cockroaches tend to cluster together at the edge of the test chamber, or around the food and water pot. The cockroaches tended to move between the side of the test chamber in a group. Dust was seen on the backs of cockroaches, presumably picked up when, as observed, they fell onto their backs. It seems likely that in some cases insects transferred dust to one another through their aggregating behaviour. Thereby cockroaches that did not themselves walk on the dust could still become dust contaminated. Clustering behaviour seemed to be more prevalent in the absence of water. Results do not give an indication about development of resistance. See footnote.	Document IIIA, Section 5.3.1.

Footnote

Mode of action: Silicon dioxide absorbs waxes from the insect's cuticle – the thin waxy protective outer layer that prevents dehydration in dry atmospheres. The loss of these waxes initiates a rapid loss of water from the insect's body, which leads to death by desiccation.

Notwithstanding the above, there is a wide variety of opinions about how inert dusts, such as silicon dioxide, bring about the rapid water loss in insects (leading to mortality). Indeed, "The Manual of Decisions for Implementation of Directive 98/8/EC Concerning the Placing on the Market of Biocidal Products" dated 30/04/2003 states that silica gel works by withdrawing water molecules from the body of the target-organism either directly due to its physical/chemical properties (strong absorption of water) or possibly by scratching the surface layer of an insects chitin protection. This position in "The Manual of Decisions" is supported by evidence reported in published literature. Given this, it is concluded that although Rentokil Initial plc report that the mode of action of silicon dioxide is absorption of waxes from the insect's cuticle leading to water loss, it is likely that silicon dioxide causes rapid water loss from insects (leading to mortality) by having a number of effects. See Document IIIA, Section 5.4 for further details regarding mode of action.

Resistance: It is known that insects with fully developed cuticles are more resistant to the action of silicon dioxide. Nymphs, whose cuticles are not fully developed are more susceptible. However, 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 reported for silicon dioxide. This is thought to be due to a combination of reasons, including the fact that sorptive dusts like silicon dioxide work by a combination of physical and chemical means (refer to Document IIIA, section 5.4.1 for details about mode of action), and sorptive dusts do not contain any chemical groups to which target arthropods are known to be resistant or apt to becoming resistant to. Indeed, sorptive dusts like silicon dioxide have been identified in literature reviews as a possible means of controlling insects that are resistant to conventional insecticides. See Document IIIA, Section 5.7 for further details regarding resistance.

3 HUMAN HEALTH EFFECTS ASSESSMENT

3.1 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Result	Reference
Absorption: The mechanism of silicon absorption from the gastrointestinal tract is not clear. However, silicon dioxide is known to be absorbed from the gastrointestinal tract as silicic acid is. It has been found that the absorption of ingested silicon compounds depends on their solubility in water. The uptake of silicon as an orthosilicic acid solution was investigated in 8 healthy volunteers. The minimum median uptake was 50.3% (range 21.9-74.7%) based on urinary analysis post-dosing. Uptake was not affected by whether the volunteers were given 27 or 55 mg silicon. It has been reported that 36% of a radio labelled Si in a silicic acid solution was absorbed and eliminated by a healthy human volunteer. In male volunteers given 2 pints of beer (containing 16.8 mg silicon) there was rapid absorption and subsequent excretion with 42-75% being excreted in the urine within 8 hours of ingestion. Serum silicon levels were markedly increased 1 hour after dosing. **Distribution:** Silicon is a component of serum, being present in the form of non proteinbound orthosilicic acid. It has been demonstrated that various human body tissues contain silica, which is present at varying levels during the life cycle. In rats given intra-cardiac injections of ^{31}silicon labelled silicic acid, one hour after dosing the highest levels were found in the kidney, liver and lungs with moderate amounts being found in bone, skin, muscle, testes and spleen. The levels then began to decline when measured 2 and 4 hours after dosing Brain tissue contained negligible amounts of silicon suggesting active exclusion by the blood-brain barrier. **Metabolism:** The metabolic pathways of silica are only partially understood with silicic acid thought to be the form present in blood. Public domain literature is in agreement that silica is absorbed through the gastrointestinal tract and excreted *via* the kidneys. **Excretion:** The kidneys play the main role in silica excretion. Silicon dioxide has been shown to be excreted as silicic acid and silicon has been shown to be excreted in urine in the form of the orthosilicic anion bound mainly with magnesium or calcium cations. In a public domain study in humans, renal clearance was 82-96 ml/min suggesting high renal filterability. In patients suffering from chronic renal failure, urinary silicon excretion was decreased and serum silicon levels increased. In a public domain study in a human volunteer, elimination of radiolabelled silicic acid indicated two simultaneous first-order processes with half-lives of 2.7 and 11.3 hours respectively. Elimination was essentially complete after 48 hours and was equivalent to 36% of the dose given. 90% of the absorbed silicon was rapidly eliminated and was probably retained in the extracellular fluid volume while the slowly eliminated silicon could represent intra-cellular silicon. Ingested silicon is also excreted *via* the faeces. Literature in the public domain demonstrates that silicon dioxide is readily excreted from the lung after inhalation. In two public domain studies in rats of subchronic inhalation, it was found that after cessation of exposure, there had been lung clearance after 13 weeks in the first study and significant decrease in lung burden after 3 months in the second. **Conclusion:** It has been shown in studies available in the public domain that silicon dioxide is innocuous under test conditions with no adverse effects or interference with essential dietary components. Therefore it is not considered scientifically necessary to carry out any further metabolism studies for silicon dioxide. **Dermal absorption:** A dermal absorption study is not considered necessary, as it is possible to consider route-to-route extrapolation from the oral metabolism data cited above which does not indicate any adverse effects that need to be examined further. There is no data to suggest that this route-to-route extrapolation would not be possible.	Document IIIA, Section 6.2

Footnotes

1. There are no metabolites of concern which are formed in mammals. It is on this basis that it is not scientifically necessary to submit additional data on metabolites of concern from carbon dioxide (the data requirements detailed in Document III-A 6.6.7).

3.2 ACUTE TOXICITY

Route	Method Guideline	Method	Species Strain Sex No/group	Dose levels Duration of exposure	Value LD_{50}/LC_{50}	Remarks	Reference
Oral	Not applicable.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	It is not considered necessary to determine the toxicity of silicon dioxide by the oral route because the principal exposure to silicon dioxide is by the inhalation route, as it is a dust, making oral exposure insignificant by comparison.	Document IIIA, Section 6.1.1
Dermal	Not applicable.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	In accordance with the TNsG, acute toxicity data has been submitted for silicon dioxide via the oral and inhalation route. Acute dermal toxicity is therefore not required under the Biocidal Products Directive.	Document IIIA, Section 6.1.2
Inhalation	No set guideline followed. Refer to "Method" for summary of methodology followed.	Refer to notes under "Remarks".	Rat: Wistar; 5 male and 5 female.	Mean actual concentration : 477mg/m³ for 4 h.	>477 mg/m^3	Data is available from one public domain study on the acute effects from the inhalation of amorphous silicon dioxide by rats. The public domain study shows that there were no mortalities and that no adverse effects occurred amongst rats exposed to 477 mg/m^3 amorphous silicon dioxide by inhalation for four hours. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18). Method: Wistar rats were housed in groups of five to a cage in an environmentally controlled room. Animals received stock diet for rats and bottled tap water ad libitum. A group of five male and five female rats were exposed for four hours to the test material (at maximum attainable concentration) in a stainless steel exposure chamber (volume: 1.5m^3). During exposure, the animals were housed individually and deprived of water and food. Immediately after exposure, the animals were returned to their living cages for an observation period of 2 weeks. During the exposure and the observation period, the rats were examined for clinical signs daily. Body weights were recorded prior to exposure and at days 1, 2, 4, 7 and 14. At the end of the observation period all animals were killed and examined for gross pathology.	Document IIIA, Section A6.1.3

3.3 IRRITATION AND CORROSIVITY

Skin irritation

Species	Method	Average score 24, 48, 72h		Reversibility yes/no	Result	Remarks	Reference
		Erythema	Edema				
Rabbit (New Zealand) .	Not a guideline study. Refer to "Method" in Remarks column.	No effects observed.	No effects observed.	Not applicable.	Non-irritating to skin.	Method: New Zealand white rabbits (male and female) were housed individually in stainless steel cages on a 12 h/day light cycle. 0.5 g of the test substance was suspended in olive oil. Both solutions were placed on a patch and then applied to both intact and scarified skin of three male and three female rabbits. The patches were removed 24 h after application and the application sites were scored for skin irritation immediately after removal of the patch and 48 h later (72 h after application). Changes in behaviour, signs of toxicity, food intake and bodyweight gain were monitored over 14 days. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18).	Document IIIA Section 6.1.4

Eye Irritation

Species	Method	Average score				Result	Reversibility Yes/no	Remarks	Reference
		Cornea	Iris	Redness Conjunctiva	Chemosis				
Rabbit (New Zealand).	Not a guideline study. See "Method" in Remarks column.	Not specified in report.	Not specified in report.	Slight.	Not specified in report.	Very slightly irritating to rabbit eye.	Yes. 1-2 days.	Method: New Zealand white rabbits were housed individually in stainless steel cages on a 12 h/day light cycle. 0.1 g of test material was instilled into the conjunctival sack of eight male rabbits. The animals were divided into two groups. Group 1 (5 animals): 5 min after instillation of test substance, the eyes were rinsed with 300 ml water for 2 min. Group 2 (3 animals): Procedure was performed 24 h after the examination of the eyeand eyes scored at 1, 24, 48 and 72 h (group 2 only) with a hand-held split lamp. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18).	Document III-A6 Section 6.1.4

3.4 SKIN SENSITISATION

Species	Method	Number of animals sensitised / total number of animals	Result	Remarks	Reference
Not applicable.	Not applicable.	Not applicable.	Not applicable.	Skin sensitisation tests assess the ability of chemicals to affect the immune system. The antigen involved is presumed to be formed by the binding of the chemical to body proteins. The antibodies that form to the ligand-protein complex give rise to an allergic reaction with subsequent exposure. The skin sensitisation reaction (as described above) is dependent on the chemical entering beneath the skin and into the blood. To try to achieve this, the OECD skin sensitisation tests, OECD 406 and OECD 429, when carried out using a powder (the form that the notified substance takes), require choice of suitable solvent for this to be possible. This does not realistically reflect what would happen if an exposure were to occur. The notified substance has low solubility in water and simply by skin contact will not be expected to dissolve (or in the process, convert to an acid form – which happens in the stomach under acid breakdown of silicon dioxide). Even if it were to be washed off the skin thus providing a solvent, any water used would most likely be saturated with silicon dioxide thus preventing dissolution of the notified substance. Notwithstanding this, the notified substance is insoluble in organic solvents (consequently it is insoluble in fat) therefore cannot enter into the skin. Therefore no skin sensitisation effect is possible due to zero exposure. Generation of test data to determine the skin sensitisation potential of silicon dioxide is therefore not necessary.	Document III-A6 Section 6.1.5

3.5 REPEATED DOSE TOXICITY

Route	Duration of study	Species Strain Sex no/group	Dose levels Frequency of application	Results	LO(A)EL	NOAEL	Remarks	Reference
Inhalation	Not applicable.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	2.4 mg/m^3 (respirable dust) See remarks.	The public domain study shows that any adverse effects to rats from the inhalation of amorphous silicon dioxide for 90 days is reversible. The UK workplace exposure limit (WEL) has been taken as the NOAEL. This data is considered suitable for the risk assessment as it is well established and set by governmental authorities.	Document IIIA, Section 6.4.3

Data is available from public domain studies on the subchronic effects of amorphous silicon dioxide on rats (see study summaries attached to Document IIIA, Section 6.4.3). The public domain studies show that any adverse effects to rats from the inhalation of amorphous silicon dioxide for 90 days is reversible. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18).

Therefore it is not considered scientifically necessary to carry out a subchronic toxicity study for silicon dioxide.

Even though this is the case for silicon dioxide, and it forms part of the justification for not submitting data on the long-term toxicity of this compound, data on the subchronic toxicity of silicon dioxide is not considered scientifically necessary for the following additional reasons:
The Biocidal Products Directive (98/8/EC, "the Directive") requires long-term testing in rodents as part of the suite of toxicology tests in order to assess the possible adverse consequences of chronic exposure (i.e. chronic toxicity and carcinogenicity) to the biocidal active substance. The Directive states in Article 8 (5) that "information which is not necessary owing to the nature of the biocidal product or its proposed uses need not be supplied. The same applies where it is not scientifically necessary or technically possible to supply the information. In such cases, a justification acceptable to the competent authority must be submitted..." A more detailed waiving concept is given in the TNsG on data requirements. In addition, the TNsG gives the strong recommendation "to minimise testing on vertebrate animals or to avoid unnecessary suffering of experimental animals the data should not be generated".
Behind this background, the waiver concept outlined in the TNsG on data requirements is considered applicable for silicon dioxide with regard to the long-term toxicity studies and therefore a scientific justification for waiving these studies are presented below.

- It is not scientifically necessary on the basis of low exposure to silicon dioxide during its normal use as a biocide.

Exposure to amorphous silicon dioxide when used as an insecticide is inconsequential because of the ubiquity of forms of silicon dioxide in the environment. Silicon, in the form of silicon dioxide and silicates (salts of the various silicic acids), occurs abundantly in nature, comprising about 25% of the earth's crust. Silicon dioxide and silicates are present in practically all plants and animals and in natural waters. Between 10 and 200 mg silicon dioxide is present in 100g dry weight of normal human tissue. The lungs and lymph nodes of older adults may have levels several times this amount. Silicon dioxide is an approved food additive, assigned the E number E551, and is used as an anti-caking agent. Silicon dioxide has been given an acceptable daily intake of "not limited". In addition, silicon dioxide is approved for use in plastic material coming into contact with food, without hazard to public health. Synthetic amorphous silicas are widely used in industry (for example as absorbents, dessicants and fillers) and in synthetic fabrics, plastics, lacquers, vinyl coatings, varnish, paper, pharmaceuticals, adhesives, foods, floor waxed, paints rubber, and inks. Estimates indicate that 4,400,000 people are exposed to amorphous silicas in their work environments. The risk assessment for human exposure to silicon dioxide, when applying the representative product RID Insect Powder, estimates exposure to be 0.0043 mg silicon dioxide/kg/day *. To put this exposure into context, and notwithstanding the information given above, the silicon dioxide content of raw potato is reported to be 10.1 mg/kg, and one litre of beer contains 131 mg.

* Refer to Document IIIA, section 2.10 for details of human risk assessment for silicon dioxide.

- In addition to the above, the potential for exposure to silicon dioxide when it is manufactured for use as an insecticide is minimal. Silicon dioxide is manufactured in a completely enclosed system, as is the manufacture of the insecticide product based on silicon dioxide. This means there is no exposure to workers, bystanders or the environment during manufacture. It is estimated that [redacted] of silicon dioxide will be manufactured each year for use as a biocide. This amount of silicon dioxide is tiny in comparison to the other non-biocidal uses of silicon dioxide. For example, amorphous silicon dioxide is the main component of glass and in 1995, 12.9 million tonnes of glass was discarded in the US alone.
  [redacted]

- Operator exposure work has been carried out in humans exposed to high concentrations of silicon dioxide. Such data has been used previously by a number of regulatory authorities to set national, international and supranational maximum exposure limits for safe working conditions, and all of these exposure limits are in general agreement. For example, the long term occupational exposure limit for silicon dioxide set in the UK is 2.4 mg/m^3 (respirable dust) (8h time weighted average). The US threshold limit value (TLV, set by the American Conference of Governmental Industrial Hygienists, ACGIH) for silicon dioxide is 2 mg/m^3 (respirable dust). In Australia, the long-term occupational exposure limit for silicon dioxide is also 2 mg/m^3 (respirable dust). The risk assessment for human exposure to silicon dioxide, when applying the representative product, RID Insect Powder shows that exposure to silicon dioxide does not exceed these agreed maximum exposure limits for safe working conditions*. As the objective of an animal test is to predict the toxicological effect in humans, then an established safe exposure level based on human data takes precedence over animal data generated for an approximation of a theoretical safe value.
  *The risk assessment for human exposure to silicon dioxide shows exposure to RID Insect Powder, under normal working conditions did not exceed the recommended UK maximum exposure limit to amorphous silicon dioxide (set at 2.4 mg/m^3 for respirable dust)**.

  ** Refer to Document IIIA, section 2.10 for details of human risk assessment for silicon dioxide.

- There is a substantial volume of information available for amorphous silicon dioxide. The data available are in general agreement, all showing that amorphous silicon dioxide *per se* is intrinsically biologically inert.

There is a substantial volume of information available for silicon dioxide, and while there are no studies available performed to specific guidelines, which consider chronic toxicity or genotoxicity specifically, it does cover all the major biological considerations. Given the large volume of data available for silicon dioxide, only the typical findings have been summarised below with regards to the chronic toxicity and carcinogenic potential of silicon dioxide. A number of reviews have been conducted by different regulatory bodies including the EPA, and the FDA, who considered the health aspects of silicon dioxide as a food additive. EPA concluded that silicon dioxide's acute toxicity profile is characterised as moderate to low, and consequently silicon dioxide has been exempted from the requirement of a tolerance limit when applied to growing crops or agricultural commodities. 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. The joint FAO/WHO Expert Committee evaluated a number of food additives. The anti-caking agent silicon dioxide was given an acceptable daily intake of "not limited". There are two FDA direct food ingredient regulations for silicon dioxide, plus a clearance by the US Department of Agriculture for its use in curing mixes and in animal feed premixes. In agreement with the review by the EPA, the FDA concluded that silicon dioxide appears to be biologically inert and there was no evidence available that suggests silicon dioxide is hazardous to humans.

Exposure to increasing concentrations of silicon dioxide: Effects and observations
Below is a summary of the long-term toxicity studies available for silicon dioxide. They are summarised in full under the relevant end points in Document IIIA.

Chronic, oral
Takizawa et al. orally administered 0, 0.125, 2.5 and 5% amorphous silica to $B_6C_3F_1$ mice and Fisher rats 93 weeks and 103 weeks respectively and found that repeated oral administration produced no significant treatment-related effects. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.5 – Study summary 1 of 1).

Chronic, inhalation

Schepers exposed Wistar rats, guinea pigs and rabbits to 126 mg/m^3 amorphous silica by inhalation for a maximum of 24 months. No radiographic signs of lung disease in animals at the end of their maximal period of silicon dioxide inhalation were found. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.5 – Study summary 1 of 2).

Choudat et al studied the health records and chest x-rays of 131 workers (male), 90 of which were the control group and 41 of which were the test group. The 41 men were exposed to 0 – 3.4 mg/m^3 respirable dust over a mean exposure period of 8 years. It was shown that the exposure to precipitated silica dust induces little respiratory impairment, which was increased by smoking. The test subject questionnaire, chest x-ray films and concentrations of arterial blood gas were used to distinguish the two groups of workers (exposed or not) None of these methods were able to discriminate. Exposure to amorphous silica dust may induce a mild small airway disease, only in comparison to a control group. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.5 – study summary 2 of 2).

Repeated dose, inhalation
Reuzel et al. exposed Wistar rats to up to 30 mg/m^3 amorphous silica by inhalation for 90 days. It was found that amorphous silicas did not induce persistent granulomas and the adverse affects in the respiratory tract partly or completely regressed. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.4 – Study summary 1 of 2).

Johnston et al. exposed Fischer-344 rats to 50 mg/m^3 amorphous silica by inhalation for 90 days. It was found that amorphous silicon dioxide did not cause gene mutation, partly because of its low biopersistence and that the effects of exposure were reversible as demonstrated by the post-exposure results. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.4 – Study summary 2 of 2).

Carcinogenicity
Takizawa et al. orally administered 0, 0.125, 2.5 and 5% amorphous silica to $B_6C_3F_1$ mice and Fisher rats 93 weeks and 103 weeks respectively and found that repeated oral administration produced no significant treatment-related effects. (Referenced and summarised in Document IIIA, Annex point IIA, 6.7 – Study summary 1 of 1).

Conclusion
It has been demonstrated that the low level of exposure to silicon dioxide during its use as an insecticide (PT18) indicates that it is not scientifically necessary to conduct a chronic toxicity study on silicon dioxide as it will not add any useful information to the risk assessment. It has been shown in the human risk assessment that compared to exposures *via* the diet and the environment, exposure from silicon dioxide as an insecticide is insignificant. The risk assessment for human exposure to silicon dioxide, when applying the representative product RID Insect Powder shows that exposure to silicon dioxide does not exceed agreed, well established maximum exposure limits for safe working conditions with silicon dioxide and nuisance dust. The toxicological profile of silicon dioxide has been well established with a large body of data available in the public domain. The operator exposure limits that have been set for nuisance particles and dusts are also based on a large amount of available data. As shown above, data is available on the effects of exposure to amorphous silicon dioxide and this data shows that there are no lasting adverse effects. Although this data has its limitations and there are no studies available which consider subchronic toxicity performed to specific guidelines, it is considered sufficient to address the toxicity of silicon dioxide particularly given the levels of exposure expected to silicon dioxide through other, non-biocidal uses of silicon dioxide including its use in food.

Footnotes
1. A 28-day repeated dose toxicity study (the data requirements detailed in Document III-A, 6.3.1, 6.3.2 and 6.3.3) is not required for silicon dioxide when an adequate 90 day study is available in a rodent.

2. A 90-day subchronic toxicity study by the oral and dermal route (the data requirements detailed in Document III-A 6.4.1 and 6.4.2) has not been submitted because a) The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products" states that the required route of administration for the subchronic toxicity test is the oral route, unless it can be justified that an alternative route is more appropriate. As silicon dioxide is a dust, the most significant route of exposure is via inhalation rather than the oral route. It is on this basis that subchronic toxicity test (oral route) is not considered necessary. b) The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data

Requirements for Active Substances and Biocidal Products" states that a percutaneous study is only required when potential dermal exposure is significant and route-to-route extrapolation is not possible. However, route-to-route extrapolation is possible from oral to dermal in this case.

3. It is not considered scientifically necessary to carry out a chronic toxicity study for silicon dioxide on the basis of the findings of the 90-day subchronic toxicity test (A6.4.3). All effects observed in the subchronic 90-day toxicity test were found to be reversible. The "Technical Guidance Document in Support of Directive 98/8/EC Concerning the Placing of Biocidal Products on the Market: Guidance on Data Requirements for Active Substances and Biocidal Products" states that data on the long-term toxicity of the active substance may not be required if the subchronic toxicity test demonstrates reversibility.

3.6 GENOTOXICITY

3.6.1 In vitro

Test system Method Guideline	Organism/ strain(s)	Concentrations tested	Result +S9 +/-/±	Result -S9 +/-/±	Remark	Reference
Not a guideline study. See "Method" in Remarks column.	*S. typhimurium* TA 1535, 1537, 98, 100 and 1538 and *E. coli* WP2.	0.033, 0.10, 0.33, 1.0, 3.3, 10 mg per plate.	No activity	No activity	Silicon dioxide has no mutation potential to bacterial cells. Method: The standard S. typherium plate-incorporation assay was performed as described by Ames et al. (1975). The test substance was dissolved in dimethyl sulphoxide and tested over a wide range of doses separated by approximately one-half log. Concurrent positive controls were run with each test, both with direct-acting mutagens and with mutagens requiring S9 activation. Test results were considered valid only if the positive control compounds induced increases in mutant counts to at least twice background. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18). Note: Two further studies have been submitted as part of Annex Point IIA, VI, 6.6.1. These studies also show there to be no genotoxic effects from amorphous silicon dioxide.	Annex Point IIA, VI, 6.6.1

Footnotes

1. It is not scientifically necessary, on the basis of *in vivo* data available, to submit additional *in vitro* genotoxicity tests under Annex Point IIA, VI, 6.6.3.

3.6.2 In vivo

Type of test Method / Guideline	Species Strain Sex No / group	Frequency of application	Sampling times	Dose levels	Results	Remarks	Reference
Not a guideline study. See "Method" in Remarks column.	Rat (Fischer-344); male; 4	Continuous: 6hday^{-1}, 5 daysweek^{-1} for 13 weeks	6.5 and 13 weeks exposure; 12 and 13 weeks post-exposure	50.4 ± 19.0 mgm^{-3} 6hday^{-1}, 5 daysweek^{-1} for 13 weeks	No effects reported.	Amorphous silicon dioxide does not cause gene mutation, partly because of its low biopersistence. Method: Three groups of rats were exposed to filtered air (control) or aerosols of silica in whole-body chambers. After 6.5 and 13 weeks exposure and 3 and 8 months of recovery, groups of rats were euthanised for analysis of lung silica burdens, cellular and biochemical bronchoalveolar lavage fluid markers of lung injury and inflammation, histopathology, inflammatory cytokine gene expression and mutagenesis in alveolar epithelial cells. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18).	Document III-A6 Section 6.6.5

Footnotes

1. It is not scientifically necessary, on the basis of the genotoxicity data available *in vitro*, to submit additional *in vivo* genotoxicity tests under Annex Points IIA, VI, 6.6.4, 6.6.5 and 6.6.6.

3.7 CARCINOGENICITY

Route	Species Strain Sex no/group	Dose levels Frequency of application	Tumours	Remarks	Reference
Inhalation	Human; male; 41 in group	Total dust ranged from 0 to 10.5 mg/m³, respirable dust ranged from 0 to 3.4 mg/m³; 8 h/day; average 8 years	No effects.	Method: The purpose of this study was to determine the pulmonary effects of occupational exposure to amorphous silica compared with a control group. Also, blood gas concentrations, at rest and during exercise, were evaluated as possible indicators of changes in lung function as a result of exposure. The study population was composed of workers at a large chemical plant engaged in the synthesis of amino acids and vitamins. Measurement of pulmonary function was carried out at the work site, using a computerised pneumotachograph Fleisch No 3 (Spiromatic, MSR) which was calibrated daily. Samples for blood gas analysis were taken from the earlobe after vasodilation with Finalgon (Boehringer Ingelheim) 10 minutes before the first incision. Arterial blood was collected and heparinised capillary tubes and immediately analysed by a trained technician with Corning 170 apparatus. Posteroanterior chest radiographs (8 x 8 cm) were obtained.	Document III-A6 Section 6.7
Inhalation	Human; sex not specified; 165 in group	<1.0 mg/m³ to >10 mg/m³; daily; average 8.6 years	No effects.	Method: The purpose of this study was to determine the pulmonary effects of occupational exposure to amorphous silica. A test group of 165 amorphous silica workers with at least one years exposure to precipitated amorphous silica (PAS) from two industrial premises were reviewed in this study. It involved analysis of medical records including annual spirometry, chest roentgenogram and most recent respiratory questionnaires. From this, forced vital capacity (FVC), forced expiratory volume (FEV_1) in one second, FEV_1/FVC ratio and maximum mid-expiratory flow (FEF_{25-75}) were obtained.	Document III-A6 Section 6.7
Inhalation	Human; male; 78 in group	3.5×10^{-7} to 0.0002 mg/cm³; daily; average 4.75 years	No effects.	Method: The purpose of this study was to determine the health effects of occupational exposure to Hi-Sil and Silene. A test group of 78 male workers employed in the manufacture and processing of Hi-Sil and Silene were reviewed. In addition annual chest x-rays were carried out on all 78 workers and detailed case studies of 2 employees were built. The case studies included extensive physical examinations and pulmonary function studies.	Document III-A6 Section 6.7
Inhalation	Human; sex not specified; 215 in group	2-100 mg/m³; daily; ≤14 years	No effects.	Method: The purpose of this study was to determine the pulmonary effects of occupational exposure to amorphous silica. The dust concentrations to which the workers were exposed varied with the place of work and the job. Concentrations were highest in the room in which the furnace reaction takes place, during the filling of the bags and during the final loading of the bags. A total of 215 persons have been examined during the period of observation and a total of 720 chest x-rays have been made. The x-ray data held was examined for adverse effects especially relating to silicosis.	Document III-A6 Section 6.7
Data is available from one public domain study on the carcinogenic effects of amorphous silicon dioxide on rats (see attached study summary). The public domain study shows that after administration in the diet for 24 months, no carcinogenic effects could be attributed to the exposure to amorphous silicon dioxide. This data is considered suitable for the risk assessment due to the similarity of the test substance and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18). A full comparison of the test substances and the silicon dioxide marketed as an insecticide is given in the attached study summary. Data is also available from several public domain studies conducted using data from humans. Although not carcinogenicity studies *per se*, pulmonary effects of inhaled silica were investigated, therefore tumours would have been reported. In the first of these studies (study summaries attached), it was found that, after a mean exposure of 8 years to inhaled silica, no tumours were formed. In a further study, it was found that after a mean					

exposure of 8.6 years to inhaled silica, no tumours were formed. Additionally, in a public domain study on inhalation exposure to humans it was found that after inhalation exposures ranging from 1 to 16 years, no tumours were formed. Finally, data from a further public domain study shows that after occupational inhalation exposure to silica of up to 14 years, no tumours were formed. In fact, in all of these studies, no adverse effects were reported.

Additionally, based on other available data, the International Agency for Research on Cancer (IARC) have concluded that amorphous silicon dioxide is not carcinogenic to animals or humans.

Therefore it is not considered scientifically necessary to carry out a carcinogenicity study for silicon dioxide.
Even though this is the case for silicon dioxide, and it forms part of the justification for not submitting data on the long-term toxicity of this compound, data on the chronic toxicity of silicon dioxide is not considered scientifically necessary for the following additional reasons:
The Biocidal Products Directive (98/8/EC, "the Directive") requires long-term testing in rodents as part of the suite of toxicology tests in order to assess the possible adverse consequences of chronic exposure (i.e. chronic toxicity and carcinogenicity) to the biocidal active substance. The Directive states in Article 8 (5) that "information which is not necessary owing to the nature of the biocidal product or its proposed uses need not be supplied. The same applies where it is not scientifically necessary or technically possible to supply the information. In such cases, a justification acceptable to the competent authority must be submitted..." A more detailed waiving concept is given in the TNsG on data requirements. In addition, the TNsG gives the strong recommendation "to minimise testing on vertebrate animals or to avoid unnecessary suffering of experimental animals the data should not be generated".

Behind this background, the waiver concept outlined in the TNsG on data requirements is considered applicable for silicon dioxide with regard to the carcinogenicity studies and therefore a scientific justification for waiving these studies are presented below.

- It is not scientifically necessary on the basis of low exposure to silicon dioxide during its normal use as a biocide.

Exposure to amorphous silicon dioxide when used as an insecticide is inconsequential because of the ubiquity of forms of silicon dioxide in the environment. Silicon, in the form of silicon dioxide and silicates (salts of the various silicic acids), occurs abundantly in nature, comprising about 25% of the earth's crust. Silicon dioxide and silicates are present in practically all plants and animals and in natural waters. Between 10 and 200 mg silicon dioxide is present in 100g dry weight of normal human tissue. The lungs and lymph nodes of older adults may have levels several times this amount. Silicon dioxide is an approved food additive, assigned the E number E551, and is used as an anti-caking agent. Silicon dioxide has been given an acceptable daily intake of "not limited". In addition, silicon dioxide is approved for use in plastic material coming into contact with food, without hazard to public health. Synthetic amorphous silicas are widely used in industry (for example as absorbents, dessicants and fillers) and in synthetic fabrics, plastics, lacquers, vinyl coatings, varnish, paper, pharmaceuticals, adhesives, foods, floor waxed, paints rubber, and inks. Estimates indicate that 4,400,000 people are exposed to amorphous silicas in their work environments. The risk assessment for human exposure to silicon dioxide, when applying the representative product RID Insect Powder, estimates exposure to be 0.0043 mg silicon dioxide/kg/day *. To put this exposure into context, and notwithstanding the information given above, the silicon dioxide content of raw potato is reported to be 10.1 mg/kg, and one litre of beer contains 131 mg.
* Refer to Document IIIA, section 2.10 for details of human risk assessment for silicon dioxide.

- In addition to the above, the potential for exposure to silicon dioxide when it is manufactured for use as an insecticide is minimal. Silicon dioxide is manufactured in a completely enclosed system, as is the manufacture of the insecticide product based on silicon dioxide. This means there is no exposure to workers, bystanders or the environment during manufacture. It is estimated [redacted] of silicon dioxide will be manufactured each year for use as a biocide. This amount of silicon dioxide is tiny in comparison to the other non-biocidal uses of silicon dioxide. For example, amorphous silicon dioxide is the main component of glass and in 1995, 12.9 million tonnes of glass was discarded in the US alone.
  [redacted]

- Operator exposure work has been carried out in humans exposed to high concentrations of silicon dioxide. Such data has been used previously by a number of regulatory

authorities to set national, international and supranational maximum exposure limits for safe working conditions, and all of these exposure limits are in general agreement. For example, the long term occupational exposure limit for silicon dioxide set in the UK is 2.4 mg/m^3 (respirable dust) (8h time weighted average). The US threshold limit value (TLV, set by the American Conference of Governmental Industrial Hygienists, ACGIH) for silicon dioxide is 2 mg/m^3 (respirable dust). In Australia, the long-term occupational exposure limit for silicon dioxide is also 2 mg/m^3 (respirable dust). The risk assessment for human exposure to silicon dioxide, when applying the representative product, RID Insect Powder shows that exposure to silicon dioxide does not exceed these agreed maximum exposure limits for safe working conditions*. As the objective of an animal test is to predict the toxicological effect in humans, then an established safe exposure level based on human data takes precedence over animal data generated for an approximation of a theoretical safe value.

*The risk assessment for human exposure to silicon dioxide shows exposure to RID Insect Powder, under normal working conditions did not exceed the recommended UK maximum exposure limit to amorphous silicon dioxide (set at 2.4 mg/m^3 for respirable dust)**.

** Refer to Document IIIA, section 2.10 for details of human risk assessment for silicon dioxide.

- There is a substantial volume of information available for amorphous silicon dioxide. The data available are in general agreement, all showing that amorphous silicon dioxide *per se* is intrinsically biologically inert.

There is a substantial volume of information available for silicon dioxide, and while there are no studies available performed to specific guidelines, which consider chronic toxicity or carcinogenicity specifically, it does cover all the major biological considerations. Given the large volume of data available for silicon dioxide, only the typical findings have been summarised below with regards to the chronic toxicity and carcinogenic potential of silicon dioxide. A number of reviews have been conducted by different regulatory bodies including the EPA, and the FDA, who considered the health aspects of silicon dioxide as a food additive. EPA concluded that silicon dioxide's acute toxicity profile is characterised as moderate to low, and consequently silicon dioxide has been exempted from the requirement of a tolerance limit when applied to growing crops or agricultural commodities. 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. The joint FAO/WHO Expert Committee evaluated a number of food additives. The anti-caking agent silicon dioxide was given an acceptable daily intake of "not limited". There are two FDA direct food ingredient regulations for silicon dioxide, plus a clearance by the US Department of Agriculture for its use in curing mixes and in animal feed premixes. In agreement with the review by the EPA, the FDA concluded that silicon dioxide appears to be biologically inert and there was no evidence available that suggests silicon dioxide is hazardous to humans.

Exposure to increasing concentrations of silicon dioxide: Effects and observations
Below is a summary of the long-term toxicity studies available for silicon dioxide. They are summarised in full under the relevant end points in Document IIIA.

Chronic, oral
Takizawa et al. orally administered 0, 0.125, 2.5 and 5% amorphous silica to $B_6C_3F_1$ mice and Fisher rats 93 weeks and 103 weeks respectively and found that repeated oral administration produced no significant treatment-related effects. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.5 – Study summary 1 of 1).

Chronic, inhalation
Schepers exposed Wistar rats, guinea pigs and rabbits to 126 mg/m^3 amorphous silica by inhalation for a maximum of 24 months. No radiographic signs of lung disease in animals at the end of their maximal period of silicon dioxide inhalation were found. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.5 – Study summary 1 of 2).

Choudat et al studied the health records and chest x-rays of 131 workers (male), 90 of which were the control group and 41 of which were the test group. The 41 men were exposed to 0 – 3.4 mg/m^3 respirable dust over a mean exposure period of 8 years. It was shown that the exposure to precipitated silica dust induces little respiratory impairment, which was increased by smoking. The test subject questionnaire, chest x-ray films and concentrations of arterial blood gas were used to distinguish the two groups of workers (exposed or not) None of these methods were able to discriminate. Exposure to amorphous silica dust may induce a mild small airway disease, only in comparison to a control group. (Referenced and

summarised in Document IIIA, Annex point IIA, VI, 6.5 – study summary 2 of 2).

Repeated dose, inhalation
Reuzel et al. exposed Wistar rats to up to 30 mg/m^3 amorphous silica by inhalation for 90 days. It was found that amorphous silicas did not induce persistent granulomas and the adverse affects in the respiratory tract partly or completely regressed. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.4 – Study summary 1 of 2).

Johnston et al. exposed Fischer-344 rats to 50 mg/m^3 amorphous silica by inhalation for 90 days. It was found that amorphous silicon dioxide did not cause gene mutation, partly because of its low biopersistence and that the effects of exposure were reversible as demonstrated by the post-exposure results. (Referenced and summarised in Document IIIA, Annex point IIA, VI, 6.4 – Study summary 2 of 2).

Carcinogenicity
Takizawa et al. orally administered 0, 0.125, 2.5 and 5% amorphous silica to $B_6C_3F_1$ mice and Fisher rats 93 weeks and 103 weeks respectively and found that repeated oral administration produced no significant treatment-related effects. (Referenced and summarised in Document IIIA, Annex point IIA, 6.7 – Study summary 1 of 1).

Conclusion
It has been demonstrated that the low level of exposure to silicon dioxide during its use as an insecticide (PT18) indicates that it is not scientifically necessary to conduct a carcinogenicity study on silicon dioxide as it will not add any useful information to the risk assessment. It has been shown in the human risk assessment that compared to exposures *via* the diet and the environment, exposure from silicon dioxide as an insecticide is insignificant. The risk assessment for human exposure to silicon dioxide, when applying the representative product RID Insect Powder shows that exposure to silicon dioxide does not exceed agreed, well established maximum exposure limits for safe working conditions with silicon dioxide and nuisance dust. The toxicological profile of silicon dioxide has been well established with a large body of data available in the public domain. The operator exposure limits that have been set for nuisance particles and dusts are also based on a large amount of available data. As shown above, data is available on the effects of exposure to amorphous silicon dioxide and this data shows that there are no lasting adverse effects. Although this data has its limitations and there are no studies available performed to specific guidelines which consider chronic toxicity or carcinogenicity, it is considered sufficient to address the toxicity of silicon dioxide particularly given the levels of exposure expected to silicon dioxide through other, non-biocidal uses of silicon dioxide including its use in food.

Crystalline material
It is well established that carcinogenicity is associated with the occupational inhalation of **crystalline** silicon dioxide. Therefore, it must be stressed that the material to be marketed for use as an insecticide (PT18) as supported by this dossier is **amorphous** silicon dioxide (with no crystalline content). The differences between crystalline and amorphous silica have been reviewed and studies conducted show that there are no associations between carcinogenicity and amorphous silicon dioxide but many between carcinogenicity and silicon dioxide with crystalline content.

3.8 REPRODUCTIVE TOXICITY

3.8.1 Teratogenicity

Route of exposure	Test type Method guideline	Method	Species Strain Sex No/group	Exposure Period	Doses	Critical effects dams Foetuses	NO(A)EL Maternal toxicity	NO(A)EL Teratogenicity Embryotoxicity	Remarks	Reference
Oral	No set guideline followed. Refer to "method" for summary of methodology followed.	Drinking water was offered ad libitum. 10 animals were in the control group and 10 animals were dosed with 500 mg/kg of the test compound which was mixed into the powder diet and adapted weekly to the food consumption and body weight gain. Food intake was measured daily and body weight gain weekly. Animals were observed daily for behavioural changes, general conditions and growth. Haemoglobin, erythrocytes, leukocytes and blood smears were examined at week 0 and then monthly (not during pregnancy and lactation). Females were mated at weeks 8 and 17. A 1 male: 5 females mating ratio was used. Treatment was continued during the breeding experiments. Progeny from both litters were examined for the presence of gross anomalies immediately after birth. Behaviour and body weight gain during lactation were monitored. Total treatment period of parental females was 6 months. 5 animals of each group were observed during an additional treatment-free period of 3 weeks. At autopsy, parental organs were weighed and macroscopic and microscopic examinations performed. After 4 weeks the pups were examined for gross pathology.	Rats (Wistar); Female; 10 per group	0-6 months	500 mg/ kg	No effects.	500 mg/kg bw	500 mg/kg bw	A dose of 500 mg/kg was concluded to be the NOEL for developmental and reproductive toxicity. This data is considered suitable for the risk assessment due to the similarity of the test substances and the silicon dioxide that will be marketed by Rentokil Initial as an insecticide (PT18).	Document IIIA, Section 6.8.1
Data is available from one public domain study on the teratogenic effects of amorphous silicon dioxide on rats (see above). The public domain study shows that there are no adverse effects to pregnant rats or their progeny at a dose of 500 mg/kg. This data is considered suitable for the risk assessment due to the similarity of the test substance and the silicon dioxide,										