

APPENDIX 1: NanoRiskCat●●●|●● Template

Literature methodology/sources of information

The following sources of information were used to fill out the NanoRiskCat●●●|●● for Silicon and Silicon dioxide:

1. Stone V, Hankin S, Aitken R, Aschberger K, Baun A, Christensen F, Fernandes T, Hansen SF, Hartmann NB, Hutchinson G, Johnston H, Micheletti G, Peters S, Ross B, Sokull-Kluettgen B, Stark D, Tran L. 2009. Engineered Nanoparticles: Review of Health and Environmental Safety (ENRHES). Available: <http://ihcp.jrc.ec.europa.eu/whats-new/enhres-final-report> (Accessed July 15, 2010)
2. Mikkelsen, S.H., Hansen, E., Christensen, T.B., Baun, A., Hansen, S.F., Binderup, M-L. 2011. Survey on basic knowledge about exposure and potential environmental and health risks for selected nanomaterials. Environmental Project No. 1370 2011. Copenhagen: Danish Ministry of the Environment. Danish Environmental Protection Agency
3. Warheit DB, Carakostas MC, Kelly DP, Hartsky MA. 1991. Four-week inhalation toxicity study with Ludox colloidal silica in rats: pulmonary cellular responses. *Fundamental Applied Toxicology* 16(3):590-601.
4. Chen Z, Meng H, Xing G, Yuan H, Zhao F, Liu R, Chang X, Gao X, Wang T, Jia G, Ye C, Chai Z, Zhao Y. 2008. Age-related differences in pulmonary and cardiovascular responses to SiO₂ nanoparticle inhalation: nanotoxicity has susceptible population. *Environmental Science & Technology* 42(23): 8985-8992.

Human hazard profile

1. **HARN: Does the nanomaterial fulfill the HARN paradigm?**

Answer: No

Arguments and explanation: To the best of our knowledge Silicon and Silicon dioxide does not fulfil the HARN paradigm

2. **Bulk – “Level A CLP”: Is the bulk form of the nanomaterial known to cause or may cause serious damaging effects?**

Answer: No

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Arguments and explanation: Silicon and Silicon dioxide is not classified in the Annex VI of Regulation (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

3. **Bulk – “Level B CLP”:** Is the bulk form of the nanomaterial classified for other less adverse effects according to the CLP?

Answer: No

Arguments and explanation: Silicon and Silicon dioxide is not classified in the Annex VI of Regulation (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

4. **Nano – Acute toxicity:** Is the specific nanomaterial known to be acute toxic?

Answer: No

Arguments and explanation:

5. **Are there indications that the nanomaterial causes genotoxic-, mutagenic-, carcinogenic-, respiratory-, cardiovascular, neurotoxic or reproductive effects in humans and/or laboratory animals or has organ-specific accumulation been documented?**

Answer: Maybe

Arguments and explanation:


- a. **Genotoxicity and mutagenicity:** A number of studies have reported observing genotoxix alterations, but the evidence is conflict (Mikkelsen et al.2010)
- b. **Respiratory tract toxicity:** A number of studies have associated SiO₂ with respiratory toxicity. For instance Warheit *et al.* (1991) exposed CD rats (nose-

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only) for 2 or 4 weeks at concentrations of 0, 10, 50, and 150 mg/m³ dried SiO₂ and results showed that exposures to 150 mg/m³ for 2 or 4 weeks produced pulmonary inflammation along with increases in BAL protein, LDH, and alkaline phosphatase values and reduced macrophage phagocytosis (Stone et al. 2010).

- c. **Cardiovascular toxicity:** Chen *et al.* (2008) investigated age-related differences in cardiovascular responses to SiO₂ nanoparticles in a study with young, adult, and old rats exposed to air containing aerosol of manufactured SiO₂ nanoparticles for four weeks. Chen et al. (2008) found that inhalation of SiO₂ nanoparticles caused cardiovascular alterations in old rats, and less change in young and adult rats, including pulmonary inflammation, myocardial ischemic damage, atrio-ventricular blockage, and increase in fibrinogen concentration and blood viscosity (Stone et al. 2010).
- d. **Neurotoxicity:** No information available
- e. **Reproductive damage:** No information available
- f. **Carcinogenicity:** No information available
- g. **Does the nanomaterial accumulate in tissue and/or organs?:** No information available

6. Overall evaluation of human hazard

We conclude that the color-code that best reflects the human hazard profile of Silicon and Silicon dioxide is  based on in vivo evidence indicating at least one nanospecific hazard.

Environment hazard profile

1. Bulk – “Level A CLP”: Is the bulk form of the nanomaterial classified as CLP Acute 1 or Chronic 1 or Chronic 2?

Answer: No

Arguments and explanation: SiO₂ is not classified in the Annex VI of Regulation (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

2. Nano – LC₅₀<10 mg/l: Is the nanomaterial in question reported to be hazardous to environmental species i.e. LC50 or EC 50 <10 mg/l?

Answer: Yes

Arguments and explanation: Adams et al. (2009) found that SiO₂ concentrations of 10 mg/L caused 70% mortality. For algae EC10, 72h were found to be 10.9 ± 4.4 mg/L and 15.0 ± 4.3 mg/L for 12.5nm and 27 nm SiO₂ nanoparticles, respectively (van Hoecke *et al.*, 2008).

3. Overall evaluation of environmental hazard

We concluded that the color-code that best reflects the environmental hazard profile of C60 is ● based on nanospecific LC50 or EC50 < 10 mg/l.