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

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-

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 phosphatasevalues 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.

APPENDIX 1: NanoRiskCat●●●|●● Template

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 – LC_{50}<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.