

## Form for submission of information specified in Annex E of the Stockholm Convention pursuant to Article 8 of the Convention

<b>Introductory information</b>	
Name of the submitting Party/observer	Crop Life International (CLI) on behalf of Makhteshim Agan Industries (MAI)
Contact details (name, telephone, e-mail) of the submitting Party/observer	Bert Volger, Consultant for Makhteshim Agan Industries (MAI) 1087 Heartsease Drive West Chester, PA 19382 bertvolger@comcast.net
Chemical name (as used by the POPs Review Committee)	<b>Endosulfan</b>
Date of submission	January 2, 2009

<b>(a) Sources, including as appropriate (provide summary information and relevant references)</b>	
(i) Production data:	
Quantity	
Location	
Other	
(ii) Uses	Endosulfan is a versatile insecticide with acaricidal properties. The product is used for controlling numerous insect pests and some mites in a wide variety of crops grown in temperate, subtropical and tropical climate zones.
(iii) Releases:	
Discharges	
Losses	
Emissions	
Other	

<b>(b) Hazard assessment for endpoints of concern, including consideration of toxicological interactions involving multiple chemicals (provide summary information and relevant references)</b>
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**Hazard endpoint – endocrine disruption:**

The UNEP/POPS/POPRC.4 Decision on Annex D screening document, E(ii) Adverse Effects states that:

“...Endosulfan has the potential to cause endocrine disruption in both terrestrial and aquatic species...”

This statement is unproven and misleading. In an assessment of all of the available data including published, peer-reviewed literature, as well as unpublished studies submitted to regulatory agencies, the weight-of-the-evidence indicates that endosulfan is not an endocrine-disrupting compound at environmentally relevant concentrations.

Plunkett L. M. (2008a). Endosulfan and endocrine disruption -Human Risk Characterization, prepared for MAI, June 2008.

**Hazard endpoint – neurotoxicity, haematological effects and nephrotoxicity:**

The UNEP/POPS/POPRC.4 Decision on Annex D screening document, E(ii) Adverse Effects states that:

“..Endosulfan causes neurotoxicity, haematological effects and nephrotoxicity, but shows no carcinogenic or mutagenic properties. Studies vary on the conclusion for teratogenic effects. “

A recently conducted Developmental NeuroToxicity (DNT) study concluded that there was no effect on reproduction parameters at any dietary level. The study involved technical-grade endosulfan which was administered via the diet from gestation day (GD) 6 through lactation day (LD) 21 to mated female Wistar rats, at nominal concentrations of 0, 50, 150 and 400 ppm. The offspring were evaluated using detailed clinical observations, body weight, food consumption, developmental landmarks for sexual maturation, automated measures of activity (figure-eight maze), auditory startle habituation, learning and memory (passive avoidance and a water maze task), and an ophthalmic examination. Tissues were collected for morphometry (brain) and microscopic examination on PND 21 (brain) and at study termination (brain, an assortment of additional neural tissues, and skeletal muscle). Lastly, sperm analysis was performed on selected control and high-dose males.

Dietary administration of endosulfan to pregnant rats at the highest tolerated dose of 400 ppm from GD 6 through LD 21 did not produce evidence of neurotoxicity in the offspring. The sperm analyses conducted with epididymal and testicular sperm (motility, sperm counts and morphology) showed no treatment related effects.

Anderson, D. G., Facey, J. (2007). Endosulfan - Developmental Neurotoxicity Feeding Study in Rats (EPA Review). Reregistration Branch 2, Health Effects Division, Office of Pesticide Programs, OPPTS, US EPA, Washington, DC. Memorandum to Tracy Perry, SRRD (7508P), D327215. TXR# 0054486; DP Barcode: D327215; MRID 46968301. Docket No.: OPP-2002-0262-0058.1, March 15, 2007. <http://www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=EPA-HQ-OPP-2002-0262>

Further, in a recently prepared overview considering all of the available data for endosulfan, **the weight-of-the-evidence indicates in detail that endosulfan does not pose a neurotoxic risk to human health, and is not an endocrine-disrupting compound at environmentally relevant levels of exposure.**

Plunkett L. M. (2008b). Endosulfan and Neurotoxicity - Human Risk Characterization, prepared for MAI, June 2008.

In the UNEP/POPS/POPRC.4/INF/14 document it was noted that: “An evaluation of that endpoint should await commonly accepted test procedures for determining effects”

Until evidence of the contrary has been shown, it seems pre-mature to classify endosulfan as a potential endocrine disruptor in both terrestrial and aquatic species. Endosulfan is not an endocrine disruptor as demonstrated in the available in-vitro and in-vivo GLP studies.

Plunkett L. M. (2008a). Endosulfan and endocrine disruption -Human Risk Characterization, prepared for MAI, June 2008.

<b>(c) Environmental fate (provide summary information and relevant references)</b>	
Chemical/physical properties	No new data
Persistence	<u>The issue of persistence of endosulfan in the environment is hereunder clarified by reference to specific environmental media.</u>  <b><u>Persistence in air:</u></b> In the EC proposal it was stated that at an elevated temperature of 75 °C a rate constant of $6 \pm 1.5 \times 10^{-13} \text{ cm}^{-3} \text{ s}^{-1}$ was determined for $\alpha$ -endosulfan in a gas-phase reaction chamber. From that number an estimated atmospheric half-life of $27 \pm 11$ days was derived for 75°C assuming an aerial concentration of $[\text{OH}] = 5 \times 10^5 \text{ cm}^{-3}$ . As two basic molecular mechanisms (H-abstraction and addition to the double bond) with an opposing temperature gradient are involved in the overall reaction of endosulfan and OH-radicals, the rate constant and consequently the half life cannot be transformed to lower temperatures. On behalf of gas phase reactions inert solvent-systems (CFC 113)

are discussed as a surrogate matrix for the atmosphere, in which to measure OH-reactivity of semi-volatile compounds. Rate constants of the test substance are thereby determined by relating the decline of the concentration of a test substance to that of a reference substance of known gas phase OH-reactivity. In such a model system employing toluene as a reference compound half-lives of > 2.7 days were found for  $\alpha$ -endosulfan (Kloepffer 1992a), and of > 15 days for  $\beta$ -endosulfan (Kloepffer 1992b). For endosulfan sulfate a half life of 2.7 days in the troposphere at minimum was determined as well (Kloepffer 1992c).

(i) UNEP/POPS/POPRC.4/INF/14, August 27, 2008

(ii) Buerkle, L.W. (2001). Endosulfan - Estimation of the reaction with photochemically produced hydroxyl radicals in the atmosphere, Aventis CropScience, Environmental Chemistry, Doc# C012614

**Comment:**

It should be noted that these half-lives were measured in the liquid phase. A transformation to the gaseous phase is difficult to perform due to the two basic molecular mechanisms since the influence of the aggregation status has not been investigated. In addition, no explanation could be given for the different results with the molecules of a similar structure. In summary, the two experimental approaches for the reaction of endosulfan with OH-radicals resulted in inconsistent half-lives, and apply only to the particular experimental conditions.

**A transformation and extrapolation of these results to natural environmental conditions is not possible for reaction-mechanistic reasons, and does not represent accurate half-lives of endosulfan in air.**

The half-life values used in the draft proposal, UNEP/POPS/POPRC.4/INF/14, are based either on an out-dated QSAR calculation method according to Atkinson (1987) with larger uncertainty intervals due to estimated increments or on values derived under very specific experimental conditions that cannot be transferred to realistic environmental circumstances.

Palm, W.-U. and Zetzsch, C. (1991). Estimation of the rate constants for the reaction of alpha- and beta-endosulfan with OH radicals by the incremental procedure of Atkinson. AgrEvo Doc. No. A48681.

Estimates conducted with AOPWIN v1.88 resulted into a photo-oxidative DT50 of 47.1 hours (1.96 days) assuming an OH• concentration of  $0.5 \times 10^6 \text{ cm}^{-3}$  in 24 hours per day and 1.3 days for an OH• concentration of  $1.5 \times 10^6 \text{ cm}^{-3}$  in 12 hours per day. There is some uncertainty surrounding the estimated DT50 in air related to the estimation method, the determination of the OH• reaction rate and variation in OH• concentration.

**However, it can be concluded that the atmospheric half-life of endosulfan is shorter than two days.**

Buerkle, L.W. (2003). Endosulfan - Evaluation of estimation and experimental methods on determination of the half-life in the atmosphere, Bayer CropScience, Metabolism/Environmental Fate, report No. C029156; MRID 46029902.

**Persistence in water:**

Hydrolysis in freshwater ( $T_{1/2} > 200$  days at pH 5) meets the POP persistence criteria. However, based on information from long-term monitoring of water bodies, the mean pH in Europe is 7.4, versus 7.3 for the US. Both regions had about 10% of the sites with a mean pH below 6. Therefore we believe it is reasonable to use pH 7 rather than a pH 5 data point as it was proposed for the LRTAP dicofol assessment.

Conklin M. et al. (2002) Regional pH and Alkalinity Patterns in GLOBE data  
[http://www.globe.gov/fsl/html/templ\\_unh1999.cgi?Conklin-R2&lang=en&nav=1](http://www.globe.gov/fsl/html/templ_unh1999.cgi?Conklin-R2&lang=en&nav=1)

**Persistence in soil/sediment:**

Besides abiotic degradation processes (e.g. hydrolysis, photolysis), biotic degradation processes can also take place in natural water systems. The biotic degradation is simulated in the laboratory by water-sediment studies with freshly sampled surface water and the corresponding sediment from non-(or at least low) contaminated natural pools, lakes or rivers. <sup>14</sup>C-Labelled endosulfan has been investigated in different water-sediment systems according to current guidelines. Endosulfan partitioned very quickly

from the water column to the sediment (DT50 ca. 1 day). Kinetic modelling of this behaviour resulted in the following degradation (not dissipation) half lives for water and sediment:  $\alpha$ - and  $\beta$ -endosulfan is 38 days and endosulfan sulphate is 58 days.

**Hammel K. (2004). Kinetic evaluation of the dissipation of endosulfan and its metabolites, endosulfan – sulfate, endosulfan-diol, endosulfan-hydroxy carboxylic acid in Aerobic Water-Sediment Systems. Bayer CropScience, report MEF-318/03, Doc. No. C042131**

Half-lives from laboratory studies in soil are generally below the POP trigger of 180 days. The cited, old, laboratory degradation study with calculated half-life values of 288 to 2,241 (Stumpf et al. 1989; see **UNEP/POPS/POPRC.4/INF/14, page 31**) is considered invalid because of experimental deficiencies. In particular the soil microbes in the small lab samples got exhausted after approximately 4 months of incubation without contact to the natural environment and continuous nutrition. In order to overcome this shortage the soil samples in a long-term study have to be refreshed accordingly. Microbial mineralization of the chlorinated bicyclic carbon skeleton (common molecular part of endosulfan and its identified metabolites) can only be attained if measures are taken to maintain the microbial activity of the soil microorganisms throughout the study period.

**(i) Stumpf, K., P. Dambach, O. Lenz (1989). Metabolism of <sup>14</sup>C-labelled Endosulfan in five soils. Hoechst AG Doc. No. A53618**

**(ii) Jonas, W. (2002). Degradation of [<sup>14</sup>C] Endosulfan in two aerobic water/sediment systems. Aventis CropScience study No. NA 019404**

In a recent soil metabolism study with endosulfan-sulfate (Schnoeder, 2002) biological activity of soil samples was maintained throughout a year by adding small amounts of new soil from the original sampling location repeatedly to the incubation flasks. The calculated half-lives for the sulphate in soil ranged from 123 to 147 days. Norbornene-<sup>14</sup>C-labelled endosulfan sulfate, known as the major soil metabolite and being slower degraded than the parent substance was used as test substance. Up to 35 % of <sup>14</sup>C-labelled CO<sub>2</sub> was mineralized after one year indicating that the norbornene structure had been degraded to a significant extent. This result is contrary to the suggestion in the EC proposal and Annex D screening document of a mineralization rate of less than 0.1%.

**(i) UNEP/POPS/POPRC.4/15, p.20**

**(ii) Schnoeder, F. (2002). [<sup>14</sup>C]AE F051327: Soil metabolism and degradation of endosulfan sulfate. Covance Laboratories, Aventis CropScience, Doc. No. C019647 and Addendum C020629, MRID 46119105.**

**In summary, a degradation half life of 7.4 to 21 days for the sum of  $\alpha$ - and  $\beta$ -endosulfan can be derived from these field data disregarding the first sampling day as this day applies for another dissipation process (volatilisation).**

**Buerkle L.W. (2002) Endosulfan – Degradation of the major soil metabolite of endosulfan, route rate of the degradation of endosulfan sulfate, Doc# C022805, Bayer CropScience, Environmental Chemistry, Report No. C012614; MRID 46029903**

Results from field dissipation studies carried out in Europe and North America resulted in soil half-lives of 26 to 169 days (US EPA 2002, Baedelt et al. 1992). There is no soil accumulation of endosulfan, even after excessively high application rates over many years. Long-term field accumulation studies with yearly application rates of 5.5 to 12.5 kg endosulfan per ha over a period of 5 to 7 years in different regions, have also shown that endosulfan dissipates within 6 months after the last application to a total residue level in the top soil (0-10 cm) of less than 0.1 ppm (Tiirmaa and Dorn 1988).

However, depending on the evaluation method used, the DT50 for endosulfan-sulfate ranged between 47 and 161 days. Until more accurate modeling is available, a DT50 of 161 days was used as a reasonable worst case for the degradation of endosulfan sulfate.

**(i) EU- Endosulfan Monograph (2003) - Addendum Annex B Volume III , December 2003, p.18;**

**<http://chm.pops.int/Convention/tabid/359/Default.aspx>**

**(ii) Baedelt, H., Idstein, H., Krebs, B. (1992). Endosulfan degradation in soil, Hoechst AG, GB C/Produktentwicklung Oekologie, Doc.# A54025, 143 p.**

**(iii) Tiirmaa, H., Dorn, E. (1988). Endosulfan - Worldwide monitoring of soil dissipation, Hoechst AG, GB C/LEA/R88/008/, Doc.# A40218, MRID 45421401, 38 p.**

**(iv) US EPA (2002). Reregistration Eligibility Decision for Endosulfan. Prevention, Pesticides and Toxic Substances (7508C), United States Environmental Protection Agency. Report no. EPA 738-R-02-013. November 2002. [http://www.epa.gov/oppsrrd1/REDS/endosulfan\\_red.pdf](http://www.epa.gov/oppsrrd1/REDS/endosulfan_red.pdf)**

<p>How are chemical/physical properties and persistence linked to environmental transport, transfer within and between environmental compartments, degradation and transformation to other chemicals?</p>	
<p>Bio-concentration or bio-accumulation factor, based on measured values (unless monitoring data are judged to meet this need)</p>	<p>With respect to bio-concentration, a new determination using the HPLC-method resulted in a log <math>K_{ow}</math> of 4.65 for <math>\alpha</math>-endosulfan, and a log <math>K_{ow}</math> of 4.34 for <math>\beta</math>-endosulfan under neutral conditions. The <math>K_{ow}</math> of endosulfan sulfate resulted in a log <math>K_{ow}</math> of 3.77, which is significantly lower than the <math>K_{ow}</math> of the parent endosulfan isomers indicating higher polarity, and consequently a lower bioaccumulation potential. The other metabolites included in the <math>K_{ow}</math> determination have even lower <math>K_{ow}</math> than endosulfan sulfate.</p> <p><b>Muehlberger, B., Lemke, G., (2004). Endosulfan and metabolites, partition coefficient 1-octanol/water (HPLC-method), endosulfan hydroxy carboxylic acid, sodium salt; endosulfan hydroxy ether; endosulfan lactone; endosulfan sulfate; endosulfan ether; beta-endosulfan, alpha-endosulfan. Bayer CropScience, Doc. No. C042001.</b></p> <p>At log <math>K_{OW}</math> values of 3.55 to 4.78, available aquatic food web bioaccumulation models suggest that dietary exposure of aquatic organisms to poorly metabolized organic chemicals would not likely be a dominant concern, although at the high end of this <math>K_{OW}</math> range, dietary exposure can begin to become significant (<math>K_{OW}</math> values above 5.5 =&gt; calculated food chain multipliers can go up to 10 and more).</p> <p>(i) Arnot, J.A. and F.A.P.C. Gobas (2004). A food web bioaccumulation model for organic chemicals in aquatic ecosystems. <i>Environmental Toxicology and Chemistry</i> 23(10):2343-2355.  (ii) USEPA (2003). Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000). Technical Support Document Volume 2: Development of National Bioaccumulation Factors. EPA-822-R-03-030. Office of Science and Technology, Office of Water, U.S. Environmental Protection Agency, Washington, DC 20460. December, 2003.  <a href="http://www.regulations.gov">http://www.regulations.gov</a>.  (iii) Fisk, A.T., De Wit, C.A., Wayland, M., Kuzyk, Z.Z., Burgess, N., Letcher, R., Braune, B., Norstrom, R., Polischuk Blue, S., Sandau, C., Lie, E., Larsen, H.J., Skaare, J.U., and D.C.G. Muir (2005). An assessment of the toxicological significance of anthropogenic contaminants in Canadian arctic wildlife. <i>Science of the Total Environment</i>. Vol. 351-352 (2005), p. 57-93.</p> <p>Long-term feeding studies in a variety of terrestrial mammals, cows, sheep, dogs, rats, and mice along with toxicokinetic studies confirm that the biological half-life of a single dose of endosulfan was 2 days. In a 28-day toxicokinetic study in rats, a steady state concentration in blood and tissues was achieved by day 23. At day 28, treatment was stopped, and at the end of the treatment-free period, residue levels in blood and tissues indicated that over 90% of the total administered dose had been eliminated.</p> <p><b>If endosulfan was bioaccumulating in mammals, no steady-state would have been reached and residue levels would have been eliminated much more slowly.</b></p> <p><b>Needham, D., Creedy, C.L., Hemmings, P.A. (1998). Endosulfan-14C Toxicokinetics in the rat following repeated daily oral administration of 1 mg/kg bodyweight for up to 28 days. AgrEvo UK Ltd. A 67138. MRID 45546201.</b></p> <p>Concerning endosulfan bioaccumulation in fish, there are several studies of varying quality available in the peer reviewed literature. Taking the unscreened data at "face value," the reported BCF values for fish ranged from approximately 20 to 11,600 (L/kg wet wt.). With the exception of one species (yellow tetra), BCFs were less than 3,000 for the remaining six fish species.</p> <p>However, once these data are screened for quality based on the criteria below, only two studies remained that provide the most reliable estimates of bioconcentration in fish.</p> <p>These 2 studies met screening criteria of:</p> <ul style="list-style-type: none"> <li>Documenting the stability of the test compound in water via use of measured concentrations in water and flow-through conditions.</li> <li>• Documenting (or likely providing sufficient time to achieve) steady state accumulation in test organisms for BCFs calculated using the ratio method.</li> <li>• Quantifying concentrations of at least the two separate parent isomers in tissue</li> </ul>

and water.

- Exposing organisms to test material below levels expected to cause adverse effects on test organisms
- Exposing organisms only to endosulfan (and not other chemical or biological stressors).

The mean BCF values derived from the two “reliable” studies ranged from 1,146 L/kg wet wt. for the sheepshead minnow, and 2,755 L/kg wet wt. for striped mullet.

**In summary, the measured BCF values are far below the POP trigger of 5,000 (1,000 to 3,000 in fish compared to 600 or less in invertebrates). In addition, the BCF predictions from bioaccumulation modelling with aquatic organisms range from 1,000 (mean prediction) to 2,400 (90<sup>th</sup> percentile).**

US EPA (2007a). Environmental Fate and Effects Division: Appendix 1 to 2007 Addendum; Environmental Fate and Ecological Risk Assessment of Endosulfan Report no. EPA 738-R-02-013. November 13, 2007. EPA-HQ-OPP-2002-0262. <http://www.regulations.gov>.

Within more realistic field studies (mesocosms, farm ponds) the measured BAFs were between 100 and 1,500.

- (i) Cornaby, B.W., Maciorowski, A.F., Griffith, M.G. (1989). Endosulfan - Fate and effects on aquatic ecosystems adjacent to agricultural fields planted with tomatoes (pond study) – assessment; Battelle Institute, N0954-5700, Doc.# A41298, MRID 41164101.
- (ii) Pennington, P.L., DeLorenzo, M.E., Lawton, J.C., Strozier, E.D., Fulton, M.H., and G.I. Scott (2004). Modular Estuarine Mesocosm Validation: Ecotoxicological Assessment of direct effects with a model compound endosulfan. *J. Exp. Mar. Biol. Ecol.* 298: 369-387.
- (iii) Rajendran, N., Venugopalan, V.K. (1991). Bioconcentration of Endosulfan in different body tissues of estuarine organisms under sublethal exposure. *Bull. Environ. Contam. Toxicol.* 46(1), 151-158.
- (iv) Schanne, C. (2002). (14C)-alpha, beta-endosulfan (AE F002671) formulated as emulsifiable concentrate (352 g/L endosulfan): Outdoor aquatic microcosm study of the environmental fate and ecological effects. Springborn Laboratories (Europe), Aventis CropScience, Doc. No. C019969.

Because of rapid elimination (Half-life of 2 - 4 days) there is no bioconcentration via the food chain and less risk of bio-accumulation.

- (i) DeLorenzo, M.E, Taylor, L.A, Lund, S.A, Pennington P.L., Strozier E.D., Fulton M.H. (2002). Toxicity and Bioconcentration Potential of the Agricultural Pesticide Endosulfan in Phytoplankton and Zooplankton, *Arch Environ. Contam. Toxicol.*, 42, 173-181.
- (ii) Vorkamp, K., Riget, F., Glasius M., Pecseli, M., Lebeuf, M., and D. Muir (2004). Chlorobenzenes, chlorinated pesticides, coplanar chlorobiphenyls and other organochlorine compounds in Greenland biota. *Science of the Total Environment* 331 (2004), p.157-175.

It appears that biomagnification of endosulfan is not significant. The calculated biomagnification factors (BMF) are near or below unity. Predicted BMF values near or below unity also occur when comparing lipid-normalized concentrations in tissue determined at higher percentiles of the distribution (e.g., 75<sup>th</sup> and 90<sup>th</sup> percentiles, lipid-normalized data not shown). Risks to piscivorous birds and mammals from exposure to endosulfan via drinking water and the aquatic diet are relatively small. **No exceedence of chronic levels of concern was indicated by this analysis.**

US EPA (2008). White Paper on Methods for Assessing Ecological Risks of Pesticides with Persistent, Bioaccumulative and Toxic Characteristics, Submitted to the FIFRA Scientific Advisory Panel For Review and Comment October 28-31, 2008; pp.221; October 7, 2008, OPP Docket 2008-0550. <http://www.regulations.gov>.

Mackay & Arnold (2005) came to similar conclusions in their review of the existing arctic monitoring data base associated with long-range transport for endosulfan. Based on the evaluation of trophic magnification profiles from different sites, and where sufficient data allow a sound analysis, there is no clear evidence of biomagnification for invertebrates to fish and fish to predatory fish. Calculated biomagnification factors (BMF) based on residue measurements for a range of Arctic species ranged from 0.056 to 64.7. Further analysis revealed that average invertebrate to fish and fish to predatory fish BMF values were very low ( $0.38 \pm 0.59$  and  $0.60 \pm 0.14$ , respectively). The average fish to mammal BMF value was 10.2. However, there is a high degree of uncertainty surrounding fish to marine mammal food chain links ( $\pm 16.4$ ).

**Therefore, it is not possible to conclude with any certainty whether there is a significant relationship between measured concentration and trophic level for**

	<p><b>endosulfan.</b></p> <p>Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301</p>
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**(d) Monitoring data (provide summary information and relevant references)**

**Long Range Transport of Endosulfan residues:**

Several publications indicate the potential for long-range transport of endosulfan residues, and findings of endosulfan in the Arctic at trace levels (ppq) in water, air and biota.

- (i) De Wit, C. A., Fisk, A. T., Hobbs, K. E., and Mir, D. C. G. (2002). Levels, trends and effects of Persistent Organic Pollutants (POPs) in the Arctic environment. AMAP Progress Report to the Arctic Council Ministerial Meeting, Inanri, Finland, 9-10 October 2002. [http://www.arctic-council.org/files/inari2002sao/amap\\_report.pdf](http://www.arctic-council.org/files/inari2002sao/amap_report.pdf).
- (ii) Halsall, C. J., Bailey, R., Stern, G. A., Barrie, L. A., Fellin, P., Muir, D. C. G., Rosenberg, B., Rovinsky, F. Y., Kononov, E. Y., and Pastukhov, B. 1998. Multiyear observations of organohalogen pesticides in the Arctic atmosphere. *Environmental Pollution* 10251-62.
- (iii) Hung, H., Halsall, C. J., Blanchard, P., Li, H. H., Fellin, P., Stern, G., and Rosenberg, B. (2002). Temporal trends of organochlorine pesticides in the Canadian Arctic atmosphere. *Environ Sci Technol* 36(5): 862-868.
- (iv) Kelly, B.C. (2006). Bioaccumulation Potential of Organic Contaminants in an Arctic Marine Food Web. Simon Fraser University. 439p.
- (v) Kelly, B. C., Ikononou, M. G., Blair, J. D., Morin, A. E., and Gobas, F. A. 2007. Food web-specific biomagnification of persistent organic pollutants. *Science* 317(5835): 236-239.

New data indicate that there is no spatial or temporal increase of endosulfan residues in the Arctic Environment. The reports do not point to a potential increase of exposure. There are no residue findings, which show repeated contamination of the annual fresh snow layer in the Arctic over several years, or an endosulfan concentration increase in the soil of higher cold altitudes. It is very uncertain that long-range transport of endosulfan occurs at relevant levels and to a significant extent (Mackay and Arnold 2005).

- (i) Hung, H., P. Blanchard, C.J. Halsall, T.F. Bidleman, Stern G., Fellin P., Muir D.C.G., Barrie L.A. Jantunen L.M., Helm P.A., Ma J., Konoplev A. (2005). Temporal and spatial variabilities of atmospheric polychlorinated biphenyls (PCBs), organochlorine (OC) pesticides and polycyclic aromatic hydrocarbons (PAHs) in the Canadian Arctic: results from a decade of monitoring. *Science of the Total Environment* 342 (2005), 119 – 144.
- (ii) Li Y.F. and R.W. Macdonald (2005). Sources and pathways of selected organochlorine pesticides to the Arctic and the effect of pathway divergence on HCH trends in biota: a review. *Science of the Total Environment* 342 (2005) 87– 106, or at [www.sciencedirect.com](http://www.sciencedirect.com)

Many reports indicate seasonal variation of concentrations, e.g. on Sable Island (240 km east of Nova Scotia at 43°57'N , 60° 00'W), during the summer aerial endosulfan concentration ( $\alpha$ - and  $\beta$ -isomer) were determined between 69 and 159 ng/m<sup>3</sup>, while for wintertime values dropped to 1.4-3.0 pg/m<sup>3</sup> (only  $\alpha$  -isomer). This high variation in the range of more than 10,000 are indicative of a close correlation with the use pattern of a pesticide, rather than an indication for a POP that is observed at a more constant level due to its persistence and reduced emission in the environment.

Bidleman, D.F., Cotham, W.E., Addison, R.F., Zinck, M.E. (1992) Organic contaminants in the Northwest Atlantic atmosphere at Sable Island, Nova Scotia 1988-89. *Chemosphere* 24, 1389-1412, (1992)

**From the available evidence and studies, there is no evidence of a bioaccumulation or magnification of endosulfan in the food web. Based on the very low exposure levels in food, water and the environment, no potential concern regarding adverse effects to human health and the environment exists.**

**(e) Exposure in local areas (provide summary information and relevant references)**

General	<p>Endosulfan is used mainly in warmer climates and the southern hemisphere.</p> <p>In view of the Arctic long-range transport assessment, the present actual endosulfan uses, and the sources or significant contributors, require a closer and more up-to-date assessment. For instance, since 2006 the endosulfan uses in Europe has vanished, in Canada the uses are not very relevant nor too in the USA, where a decrease from 400 t in mid 1990s and early 2000 to less than 100t in 2007 has been noted. <u>Therefore, there is less potential for actual exposure and contribution to long-range transport.</u></p>
As a result of long-range environmental transport	<p><b>Analytical Uncertainties and QA issues:</b></p> <p>It should also be noted that there is a high degree of uncertainty concerning the interpretation and significance of the monitoring data. In fact, many of the published data are of poor analytical quality (10 to 20-fold difference between the mostly used GC/ECD method and the more accurate GC/MS method), are based on very limited number of samples, and reflect high seasonal and spatial variation in endosulfan concentrations.</p> <p>Kelly, B.C. (2006). Bioaccumulation Potential of Organic Contaminants in an Arctic Marine Food Web. Simon Fraser University. 439 p.</p> <p>The validity of the published monitoring data at these very low trace levels (lipids at</p>

pg g<sup>-1</sup> to ng g<sup>-1</sup> levels, water at the pg to the low ng L<sup>-1</sup> levels, and air at pg m<sup>-3</sup> to ng m<sup>-3</sup>) need further independent analytical verification.

Lack of confirmation of results by GC-MS represents a major analytical limitation. Problems due to interfering chromatographic peaks are particularly acute for marine mammals, where clear interferences with  $\alpha$ -endosulfan from chlordane and/or toxaphene components for the ECD compared with GC-NIMS and GC-HRMS exist. Also high values obtained by GC-HRMS for  $\beta$ -endosulfan are difficult to reconcile with other results e.g. by GC-NIMS. Overall, the uncertainty in  $\alpha$ -,  $\beta$ - and –sulfate is of the order of 10x concerning the calculations of TMFs, BMFs and BAFs. There are also uncertainties in endosulfan concentrations in fish and invertebrates based on limited GC-NIMS confirmation.

**Therefore, the validity of the published monitoring data at very low trace levels (lipids at pg g<sup>-1</sup> to ng g<sup>-1</sup> levels, water at the pg to the low ng L<sup>-1</sup> levels, and air at pg m<sup>-3</sup> to ng m<sup>-3</sup>), need further independent analytical verification.**

Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301.

**Air monitoring:**

According to the AMAP Assessment (2002) endosulfan may be transported via air currents to remote areas.

AMAP (2004): AMAP Assessment 2002: Persistent Organic Pollutants in the Arctic. Arctic Monitoring and Assessment Program Assessment (AMAP), Oslo, Norway, XVI. 310p.  
<http://www.amap.no/assess/AP2002POPs.pdf>

Long-term continuous air sampling is available for comparatively few sites. The Alert site in the Canadian high Arctic provides by far the most significant and highest value dataset. From this it can be concluded that the temporal trend in endosulfan residues in the air in the Arctic appears to be stable and in agreement with its actual use between 1990 and 2000. A distinctive seasonal profile (summer reductions in  $\alpha$ -endosulfan concentrations with spring and fall peaks) probably results from a combination of complex environmental fate processes.

Hung, H., P. Blanchard, C.J. Halsall, T.F. Bidleman, Stern G., Fellin P., Muir D.C.G., Barrie L.A. Jantunen L.M., Helm P.A., Ma J., Konoplev A. (2005). Temporal and spatial variabilities of atmospheric polychlorinated biphenyls (PCBs), organochlorine (OC) pesticides and polycyclic aromatic hydrocarbons (PAHs) in the Canadian Arctic: results from a decade of monitoring. *Science of the Total Environment* 342 (2005), 119 – 144.

Some of the older results generated with a GC/ECD instead of a GC/MS analytical method, showed significant interferences as a confounding factor (e.g. co-elution from other analytes). No spatial or temporal trend of endosulfan concentrations in the environment of the Arctic is observed.

Key studies conducted in the Canadian sub-Arctic (Tagish, Yukon) have been interpreted with air mass back trajectories to assess potential sources of contaminants into the western Canadian Arctic and other Canadian monitoring sites. This research indicates that continental/southerly air masses in North America are likely to be more significant contributor to Arctic contamination.

It is apparent that the network of long-term, continuous air monitoring sites in the Arctic remains extremely limited and, as a consequence, significant spatial gaps and uncertainties remain. The NCP (Northern Contaminants Programme) air monitoring station in Alert in the Canadian high Arctic is the most robust dataset available. The vast majority of air monitoring of endosulfan conducted to-date has been focused upon  $\alpha$ -endosulfan. The mean levels are very low amounting to approximately < 1 – 15 pg/m<sup>3</sup>. There is evidence to suggest that  $\beta$ -endosulfan residues in air are comparatively minor (at least a factor of 10 below  $\alpha$ -endosulfan). Endosulfan sulfate does not appear to have been considered in typical air monitoring campaigns. The endosulfan concentrations found in monitoring studies are typically very small, resulting in significant analytical challenges. The measured concentrations often follow seasonal trends that mirror use patterns in source regions near by. The temporal trend in endosulfan residues in the air in the Arctic appears to be stable in agreement with its actual use between 1990 and 2000. Significant seasonal variation in air residues is

noted with summer reductions in  $\alpha$ -endosulfan levels of between a factor of 3-5 relative to spring and fall peaks. The seasonal profile probably results through a combination of processes ranging from the results of complex environmental processes (e.g. enhanced photochemical depletion with the onset of solar sunrise) to scavenging via vegetation ('forest filter effect') during long-range transport (consistent with Hung, et al., 2002).

(i) Li, Y.F., Macdonald, R.W. (2005). Sources and pathways of selected organochlorine pesticides to the Arctic and the effect of pathway divergence on HCH trends in biota: a review. *Science of the Total Environment* 342 (2005), p. 87 – 106.

(ii) Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301.

Overall, it should be noted that the reported concentrations in the air are far below the inhalative toxicity levels to mammals. **The highest reported single peak (3.7 ng/m<sup>3</sup>) is by at least 6 orders of magnitude lower than the acute inhalative toxicity level (rat LC50 inhalation = 12.6 µg/l air).**

#### **Water monitoring:**

The highest endosulfan levels reported were found in water samples from temperate lakes in south-central Canada at mean concentrations ranging from 1.3 to 28.5 pg L<sup>-1</sup>.

Muir, D.C.G, Teixeira, C., Wania, F. (2004). Empirical and modeling evidence of regional atmospheric transport of current use pesticides. *Env. Toxic and Chem.* 23, 2421 – 2432.

The available seawater monitoring database does not constitute a robust database that would allow firm conclusions regarding temporal trends. MacKay and Arnold (2005) concluded that complete reliance on monitoring data during the summer months in ice-free areas has additional implications regarding the understanding of environmental fate in the Arctic since it is not possible to evaluate seasonal variation due to shut down of the air-sea gas exchange process when the ice pack is present.

Concerning the spatial trends, there is a relatively high degree of analytical consistency with endosulfan concentrations in seawater typically ranging from approximately < 1 to 10 pg/L. There are no residue findings, which show repeated contamination of the annual fresh snow layer in the Arctic over several years, or an endosulfan concentration increase in the soil of higher cold altitudes. **It is very uncertain that long-range transport of endosulfan occurs at relevant levels and to a significant extent.**

Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301.

#### **Biota monitoring:**

Detailed analysis of temporal trends in biota was not possible due to the absence of long-term, site-specific monitoring campaigns data that would allow for detailed re-interpretation. However, in one study (Stern and Ikonomou, 2003) it was concluded that endosulfan sulfate residues were increasing in male beluga whales from the Canadian Arctic. There remain significant uncertainties surrounding analytical differences between this study and a more recent study conducted by Kelly (2006), which suggests lower endosulfan residues may be present when analysis is conducted by GC-MS. Difficulties with interpretation of biota measurements arise due to former reliance on GC-ECD with associated potential for analytical interference. In particular, the reported differences of results between earlier used GC-ECD and more recently applied GC-MS methods warrant further investigation and caution in interpretation.

**Overall the uncertainty in  $\alpha$ -,  $\beta$ -endosulfan and –sulfate is of the order of 10x in the case of marine mammals.**

(i) Kelly, B.C. (2006). Bioaccumulation Potential of Organic Contaminants in an Arctic Marine Food Web. Simon Fraser University. 439 p.

(ii) Stern G, Ikonomou MG. (2003). Temporal trends of organochlorine contaminants in SE Baffin (Pangnirtung) beluga, 1982-2002. Synopsis of Research conducted under the 2001-2003 Northern Contaminants Program. Ottawa ON, Indian and Northern Affairs Canada: 358-361.

Residues of  $\alpha$ -endosulfan were significantly higher in whales from the North Sea, potentially reflecting a 'near source' influence and highlighting potential confounding influences for migratory species. Spatial variation in residues of  $\alpha$ -endosulfan in biota

	<p>was specifically considered for ringed seal blubber and minke whales. In ringed seals, the highest concentrations of <math>\alpha</math>-endosulfan were found in the western Canadian Arctic and at Barrow, Alaska. There appears to be no reliable relationship to endosulfan concentrations in seawater.</p> <p>Even if the reported endosulfan concentrations are real, the values are far below values that would be expected to produce any ecological or human health effects.</p> <p><b>Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301.</b></p> <p><b>In summary, the off-site movement and long range transport requires a thorough analysis of the current monitoring data, including its scientific validity and integrity, before a proper risk assessment can be conducted.</b></p>
<p>Information regarding bio-availability</p>	<p><b><u>Ecotoxicological risk:</u></b> The Annex D screening document (UNEP/POPS/POPRC.4/15, p.22) states that there is sufficient evidence that endosulfan meets the criterion for adverse effects. This statement is unproven and not correct for the following reasons:</p> <p>As the worst case, taking the highest measured concentration from a lake in southern Canada at 0.0000285 ppb (Muir et al. 2004), and comparing this level (highest reported findings in seawater) to the lowest toxicity level for aquatic species, i.e. chronic NOEC (fish full life cycle test, 260 days) = 56,000 pg/l or 0.056 ppb (Dionne 2002), the calculated Risk Quotient (RQ) would be 0.00051, <u>which is far below of any level of concern.</u></p> <p><b>As stated by Fisk et al. (2005), endosulfan concentrations in arctic terrestrial wildlife, fish and seabirds are below effect threshold levels.</b></p> <p>(i) Muir, D.C.G, Teixeira, C. , Wania, F. (2004). Emperical and modeling evidence of regional atmospheric transport of current use pesticides. <i>Env. Toxic and Chem.</i> 23, 2421 – 2432. (ii) Fisk, A.T., De Wit, C.A., Wayland, M., Kuzyk, Z.Z., Burgess, N., Letcher, R., Braune, B., Norstrom, R., Polischuk Blue, S., Sandau, C., Lie, E., Larsen, H.J., Skaare, J.U., and D.C.G. Muir (2005). An assessment of the toxicological significance of anthropogenic contaminants in Canadian arctic wildlife. <i>Science of the Total Environment.</i> Vol. 351-352 (2005), p. 57-93; (iii) Dionne, E. (2002). Endosulfan – Chronic Toxicity to the Fathead Minnow (<i>Pimephales promelas</i>) during Full Life-Cycle Exposure. Springborn Smithers –Study No. 13726.6140; Bayer CS - Doc. No. B004189</p> <p>Further, MacKay &amp; Arnold (2005) found that the No-Observed-Adverse-Effect-Levels (NOAEL) for endosulfan in aquatic, avian and mammalian tests are orders of magnitude above the published exposure concentrations. A relatively robust evaluation of ecotoxicological risks, was facilitated through access to a very large database of effects studies, concluded:</p> <ul style="list-style-type: none"> <li>• There is essentially negligible risk to marine organisms from acute and chronic exposures to endosulfan residues in Arctic marine systems.</li> <li>• The toxicity value for the most sensitive animal was about three orders of magnitude greater than the highest measured concentration for Arctic marine waters.</li> <li>• There is similarly a negligible risk to terrestrial animals from exposures to endosulfan residues.</li> </ul> <p>Therefore, in view of endosulfan’s relatively low bioaccumulation in aquatic and terrestrial organisms, the potential risk to biological receptors seems insignificant.</p> <p><b>Mackay, N., Arnold, D. (2005). Evaluation and interpretation of environmental data of endosulfan in arctic regions, Cambridge Environmental Assessments, Report No. CEA.107, MRID 46734301.</b></p> <p><b><u>Human dietary risk:</u></b> The US-EPA recently noted the following:</p> <p><i>“Since endosulfan has routinely been detected in arctic regions and the Indigenous Peoples of the arctic region of the U.S. (Alaska) rely heavily on subsistence diets (i.e. - fish) as their food source, it is appropriate for the Agency to consider dietary risk and exposure to this specific population subgroup from the worldwide use of endosulfan.”</i></p> <p><b>Wilbur, D., Reaves, E., Facey, J., Nielson, A., Recore, S. (2007). Endosulfan - The Health Effects Division's Addendum and Update to the 2002 Risk Assessment. Reregistration Branch II, Health</b></p>

Data on the consumption of traditional foodstuffs by people residing in the Arctic region is available. The Centre for Indigenous Peoples' Nutrition and Environment (CINE) conducted three major studies of dietary intake in Arctic communities of Canada from the late 1980s to the late 1990s. The objectives of the studies were to understand the patterns of traditional food use as well as assessing the benefits and risks of using traditional food. The studies were conducted in a manner similar to the diet studies in the U.S. that EPA has relied upon. They used 24-hour food recall surveys of individuals in randomly selected households from 44 communities in three different cultural areas (the Yukon First Nations, Dene and Metis, and Inuit). A total of 3,689 interviews were conducted and more than 700 food samples were collected.

The traditional food items most often consumed included moose, caribou, whitefish, char, seal, trout, salmon, coney, goose, musk ox, crowberry, and partridge. Traditional food ranged from 6-40% of the food use as a percent of total dietary energy. The highest food intake level was for males greater than 61 years old in the Dene and Metis communities with a geometric mean consumption of 528 grams per day and a 99.9th percentile consumption of 715 grams of traditional food per day (with the 99.9th percentile calculated from the geometric mean and standard deviation). Males 0-12 years old consumed an average of 150 grams of traditional food per day.

The data collected in these interviews should be considered sufficient for the assessment of potential dietary risk for the population residing in the Arctic from endosulfan. Using this *traditional food consumption* data base, it has been shown that the potential exposure to endosulfan by indigenous people is below any level of concern. For example, the highest measured concentration in an Alaskan fish monitoring publication was 0.068 ppb in chum (EPA-HQ-OPP-2008-0615). In this survey endosulfan was not detected in over 75% of all the tissue samples collected and analyzed. However, if the highest measured concentration of 0.068 ppb were assumed to be in all traditional foods eaten by indigenous people, the dose for an adult male greater than 61 years of age would be  $7 \times 10^{-7}$  mg endosulfan/kg body weight. Based on this worst-case scenario the Margin of Exposure (MOE) is greater than 21,000. This same concentration results in a dose of  $1 \times 10^{-6}$  mg/kg for a 10 kg child providing an MOE greater than 14,000.

Hunter Youngren S. (2008). Assessment of "Traditional Food" Diets in the Arctic, prepared for MAI, September 2008. EPA-HQ-OPP-2002-0615. <http://www.regulations.gov>.

**Overall, considering very conservative assumptions, e.g. all traditional food eaten is contaminated with the highest concentration of endosulfan detected: the calculated potential risks are negligible.**

Typically not all of the food consumed is contaminated with endosulfan residues, particularly if the 99.9th percentile consumption value is used (as was done for the adult male). Moreover, it is not realistic that all of the food would have the highest residue level found, particularly when it was found in less than 75% of the samples.

The Alaska Department of Environmental Conservation concluded that based on the available fish monitoring surveys:

- Organochlorine contaminant concentrations in Alaska fish are low, and are not expected to cause adverse health effects in even the most frequent fish consumers.
- The Alaska Division of Public Health continues to recommend the unrestricted consumption of fish from Alaska waters.
- Ongoing monitoring is needed to better understand the factors influencing contaminant concentrations in Alaska fish and wildlife, actual exposure levels in humans who consume wild foods, and trends in contaminant concentrations over time.

Alaska Department of Environmental Conservation Fish Monitoring Program: Analysis of Organic Contaminants at 22, EPA-HQ-OPP-2008-0615-0002. <http://www.regulations.gov>.

**(f) National and international risk evaluations, assessments or profiles and labelling information and hazard classifications, as available (provide summary information and relevant references)**

In November 2007, the USEPA issued an updated risk assessment for endosulfan (amendment to the 2002 RED):

US EPA (2007B). Endosulfan Updated Risk Assessments, Notice of Availability, and Solicitation of Usage Information. Federal Register 72(221): 64624 - 64626. November 16, 2007. Docket Identification Number EPA-HQ-OPP-2002-0262. <http://www.regulations.gov>.

The registrant's response to this assessment was submitted in February 2008:

Volger, B. (2008). Response to USEPA's Federal Register Notice: (Volume 72, Number 221, Page 64624-4626). Requesting Public Comments on EPA's update Human Health and Ecological Effects Risk Assessments for Endosulfan. MRID 47349001, February 15, 2008. Docket Identification Number: EPA-HQ-OPP-2002-0262. <http://www.regulations.gov>.

#### **(g) Status of the chemical under international conventions**

No new data

#### **Summary Remarks**

The present endosulfan risk profile provides robust evidence that adverse human health and/or environmental effects resulting from potential long-range environmental transport are unlikely to take place. The information furnished here demonstrates that endosulfan does not meet the POP criteria and provides sufficient contrary evidence and data to the hazard and alleged human and environmental concerns cited in the POPRC proposal POPRC.4/14. In particular:

- The weight-of-the-evidence indicates in detail that endosulfan does not pose neurotoxic risk to human health, and is not an endocrine-disrupting compound at environmentally relevant levels of exposure.
- It is not persistent in air - the atmospheric half-life of endosulfan is shorter than two days.
- Its persistence in water and soil/sediment requires closer examination of the available evidence as indicated in this submission.
- With respect to bioconcentration/bioaccumulation the measured BCF values are far below the POP trigger of 5,000 (1,000 to 3,000 in fish compared to 600 or less in invertebrates). In addition, the BCF predictions from bioaccumulation modelling with aquatic organisms range from 1,000 (mean prediction) to 2,400 (90<sup>th</sup> percentile).
- Available studies and reviews suggest that it is not possible to conclude with any certainty whether there is a significant relationship between measured concentrations and trophic levels for endosulfan.
- Based on the very low exposure levels in food, water and the environment, no potential concern regarding adverse effects to human health and the environment exists.
- Concerning Long Range Transport, analytical uncertainties and quality assurance issues need to be taken into account when assessing the relevant data available. It should also be noted that there is a high degree of uncertainty concerning the interpretation and significance of the monitoring data available. In fact, many of the published data are of poor analytical quality. It is very uncertain that long-range transport of endosulfan occurs at relevant levels and to a significant extent.
- Concerning ecotoxicological risks, endosulfan concentrations in arctic terrestrial wildlife, fish and seabirds are below effect threshold levels.
- Concerning human dietary risk with respect to indigenous peoples in the Arctic, even considering very conservative assumptions, e.g. all *traditional food* eaten is contaminated with the highest concentration of endosulfan detected; the calculated potential dietary risks are negligible.