Summary of the

Proposal for listing

Endosulfan

in the Stockholm Convention

on Persistent Organic Pollutants

Introduction

Endosulfan, a synthetic organochlorine compound, is widely used as an agricultural insecticide. It was introduced into the market already back in the mid 1950s but plant production products containing endosulfan are still used in a number of countries worldwide. In scientific literature a huge number of information is available, dealing with (eco)toxicity, environmental fate, residues in food and feedstuff, environmental concentrations, etc. of Endosulfan. In addition a number of various reviews were published during the last decade.

This dossier focuses solely on the information required under paragraphs 1 and 2 of Annex D of the Stockholm Convention and it is mainly based on the following documents:

- US EPA's re-registration eligibility decision (RED)[1].
- Toxicological profile for endosulfan published by the U.S. Department of Health and Human Services[2].
- Final review of endosulfan by the Australian National registration authority for agricultural and veterinary chemicals[3].
- EU DAR of endosulfan for inclusion on Annex I of Directive 91/414/EEC[4].

These extensive review reports also serve as a source of further information referred to in paragraph 3 of Annex D of the Stockholm Convention on this candidate POP chemical.

1 Identification of the chemical

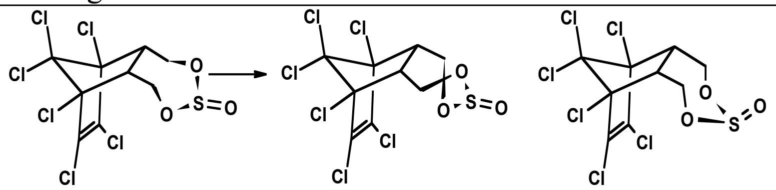
1.1 Names and registry numbers

common name	endosulfan	
IUPAC	6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide	
Chem. Abstracts	6,9-methano-2,4,3-benzodioxathiepin-6,7,8,9,10,10-hexachloro-1,5,5°,6,9,9-hexahydro-3-oxide	
CAS registry numbers	• alpha (α) Endosulfan	959-98-8
	• beta (β) Endosulfan	33213-65-9
	• technical * Endosulfan	115-29-7
	• Endosulfan sulfate:	1031-07-8
	* stereochemically unspecified	
trade name	Thiodan® , Thionex, Endosan, Farmoz, Nufarm, Endosulfan	

* technical endosulfan is a 2:1 to 7:3 mixture of the α- and the β-isomer.

1 http://www.epa.gov/oppsrrd1/REDs/endosulfan_red.pdf
2 http://www.atsdr.cdc.gov/toxprofiles/tp41-p.pdf
3 http://www.nra.gov.au/chemrev/prsendo71.pdf
4 to be published by the Spanish Authorities

1.2 Structures

formula	$C_9 H_6 Cl_6 O_3 S$
molecular mass	406.95 g/mol
structural formulas	 **first twist chair form** **second twist chair form** **alpha-endosulfan, AE F052618 (asymmetrical,** indistinguishable under ambient environmental conditions) **beta-endosulfan, AE F052619 (symmetrical)**

2 Persistence

In the environment, endosulfan is oxidized in plants and in soils to form primarily endosulfan sulfate and endosulfan-diol[5]. Formation of endosulfan sulfate is mediated essentially by micro-organisms, while endosulfan-diol was found to be the major hydrolysis product. Microbial mineralisation is generally slow.

Given a comparable toxicity of the sulfate metabolite a number of authors make use of the term "endosulfan(sum)" which includes the combined residues of both isomers of the parent and endosulfan sulfate.

In five different soil types, under aerobic conditions, DT_{50} values of 12 to 39 d (mean: 27.5 d) and 108 - 264 d (mean of 157 d) were determined for the α-isomer and β-isomer, respectively. Encompassing both isomers and the metabolite endosulfan sulfate ("total endosulfan") values of 288 to 2,241 days resulted for DT_{50}[6].

Half-lives in acidic to neutral soils range from one to two months for α-endosulfan and from three to nine months for β-endosulfan under aerobic condition. The estimated half-lives for the combined toxic residues (endosulfan+ endosulfan sulfate) ranged from roughly 9 months to 6 years[7]. Anaerobic conditions may considerably extend half-lives in soils.[8]

In two tropical soils from Brazil dissipation half-lives of endosulfan (total endosulfan) were determined to > 161 and 385 days[9].

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[5] Goebel H *et al.* . Properties, effects residues and analysis of the insecticide endosulfan. Residue Rev. 83, 1-165, (1982).

[6] Stumpf, K. *et al.* Metabolism of 14C-labelled Endosulfan in five soils. Hoechst AG Doc. No. A53618, unpublished report, (1989).

[7] US Environmental Protection Agency (EPA). EPA 738-R-02-013, November 2002. http://www.epa.gov/oppsrrd1/reregistration/endosulfan/finalefed_riskassess.pdf

[8] Sethunathan N. *et al.* Persistence of endosulfan and endosulfan sulfate in soil as affected by moisture regime and organic matter addition. Bull. Environ. Contam. Toxicol. 68, 725-731, (2002).

[9] Laabs, V. *et al.* Fate of ^{14}C-labelled soybean and corn pesticides in tropical soils of Brazil under laboratory conditions. J. Agric. Food Cehm. 50, 4619-4627 (2002).

Hydrolytic breakdown of endosulfan is enhanced with increasing pH resulting in DT_{50} of 10-20 days at pH 7 and around 0.2 days at pH 9 (at 25 °C)[10]. In alkaline sea water hydrolysis is deemed to be the main degradation process.

Photochemical transformation does not contribute to environmental breakdown in water since endosulfan does not absorb solar radiation of the troposphere (wavelengths > 290 nm). No indication for potential photo-transformation in natural water bodies could be made available from literature.

3 Bioaccumulation

Reported values for measured BCF of endosulfan in various aqueous organisms cover a wide range. In some species like oysters and bivalves BCF values as low as < 100 are reported[11], while on the other end studies on freshwater as well as marine fish suggest bioconcentration factors from 2,400 up to 11,000 in whole fish[12].

4 Potential for long-range environmental transport

There is much information available from studies on volatile soil losses to basically support the presence of endosulfan at distant sites and as a global pollutant[13].

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[10] To be added [178]

[11] Rajendran, N., V.K. Venugopalan. Bioconcentration of Endosulfan in different body tissues of estuarine organisms under sublethal exposure. Bull. Environ. Contam. Toxicol. 46(1), 151-158, (1991).

[12] - Schimmel, S.C *et al.* Acute toxicity to and bioconcentration of endosulfan in estuarine animals. In: Aquatic Toxicology and Hazard Evaluation, edited by F.L. Mayer, J.L. Hamelink, 1st Symp. ASTM STP 634, Philadelphia (PA), 241-252, (1977).

- Hansen, D.J., G.M. Cripe. Interlaboratory comparison of the Early Life-Stage Test using sheephead minnows (Cyprinodon variegates). In: Aquatic Toxicity and Risk Assessment, edited by M.A. Mayes, M.G. Barron. 14th vol., American Society for Testing and Materials (ASTM) STP 1124, Philadelphia (PA) 14, 354-375 (1991).

- Toledo, M.C.F., C.M. Jonsson. Bioaccumulation and elimination of endosulfan in zebra fish (*Brachydanio rerio*). Pest. Sci. 36(3) 207-211, (1992)

- Jonsson, C.M., M.C.F. Toledo. Bioaccumulation and elimination of endosulfan in the fish Yellow Tetra (*Hyphessobrycon bifasciatus*). Bull. Environ. Contam. Toxicol. 50(4), 572-577, (1993).

- De la Cruz, A.A., J.D. Yarbrough. The role of aquatic weeds in maintaining surface water quality. Proj.No. A-134-MS, U.S.D.I, Water Resour. Res. Inst., Missssissippi State Univ. (1982), quoted from AQUIRE Database of U.S. EPA.

[13] - Ruedel, H. Volatilization of pesticides from soil and plant surfaces. Chemosphere 35 /1/2) 143-152, (1997).

- Ruedel, H. Testing of volatility of 14C-endosulfan (formulated as the product Thiodan 35): Volatilisation from soil. AgrEvo Doc. No. A56571, unpublished results, (1992).

- Ruedel, H. Testing of volatility of 14C-endosulfan (formulated as the product Thiodan 35): Volatilisation from plant surfaces. AgrEvo Doc. No. A49663, unpublished results, (1992)

- Ahmad, N., V. Edge, P. Rohas. Aerial Transport of Endosulfan. Proc. Annual Program Workshop, Minimising the Impact of Pesticides on the Riverine Environment, Sydney, 22-23 August 1995. Land and Water Resources Research and Development Corporation. quoted in http://www.atsdr.cdc.gov/toxprofiles/tp41-p.pdf.

- Leys, J.F. et al. Anthropogenic dust and endosulfan emissions on cotton farm in northern New South Wales , Australia. Sci. Tot. Environ. 220, 55-70 (1998).

- Balluff, M. Field Soil Dissipation of AE F002671 (Endosulfan) following a single application to bare (preemergence) cotton plots at 1 location in Greece. Aventis Crop Science Study 20003033/GR1-FS (2001).

An atmospheric half-life of 27 d (± 11 days) was estimated at 75 C based on concentration of [OH] = 5 x 10^5 cm^{-3} in an experiment using a direct measurement techniques[14]. Taking into account much lower temperatures of the troposphere, environmental half life of endosulfan might even be longer. Half-lives of > 2.7 days were found for α-endosulfan[15] and of > 15 days for β-endosulfan[16] in an experiment using an indirect measurement technique.

Evidence for long range transport of endosulfan and endosulfan sulfate is provided from a number of literature sources reporting concentrations in various environmental media from Arctic regions. Concentrations of endosulfan from Arctic air monitoring stations increased from early to mid-1993 and remained at that level through the end of 1997 at 0.0042-0.0047 ng/m^3. [17] Endosulfan was measured repeatedly in Arctic seawater during the 1990s. Mean concentrations were similar to those of chlordane and ranged from 2-10 pg/L[18].

Endosulfan was detected in adipose tissue and blood of polar bears from Svalbard. Mean values found for α-endosulfan were 3.8 ± 2.2 ng/g wet weight and 2.9 ± 0.8 ng/g for β-endosulfan[19]. Endosulfan has also been detected in blubber of minke whale[20] and in liver of northern fulmar[21].

Recent modelling data of EMEP Meteorolocical Synthesizing Centre East show that once released in Central Europe endosulfan, may spread out over the Northern Atlantic reaching areas of Greenland[22].

5 Adverse effects

Endosulfan is a very toxic chemical for nearly all kind of organisms. Metabolism occurs rapidly, but the oxidised metabolite endosulfan sulfate shows an acute toxicity similar to that of the parent compound. In contrast, endosulfan-diol, which is another metabolite of endosulfan is found substantially less toxic to fish by about three orders of magnitude.

Numerous test results on effects of endosulfan and endosulfan sulfate on fish and aqueous invertebrates are available. The pattern of study results clearly establishes a high toxicity of

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[14] Zetzsch, C. Photochemisch-oxidativer Abbau von alpha-Endosulfan in der Gasphase. AgrEvo Doc. No. A48146, unpublished results (1992).
[15] Kloepffer, W. Determination of the KOH rate constant of alpha-endosulfan according to the Freon 113 method. AgrEvo Doc. No. A49537, unpublished report (1992).
[16] Kloepffer, W. Determination of the KOH rate constant of beta-endosulfan according to the Freon 113 method.. AgrEvo Doc. No. A49538, unpublished report (1992).
[17] Meakin, S. What´s New with POPs Research in the Arctic Northern Perspectives 26 (1), 6-7 (2000).
[18] Indian and Northern Affairs Canada (INAC). The Canadian Arctic Contaminants Assessment Report II (CACAR II), (2002).
[19] Gabrielsen G.W *et al.* Halogenated organic contaminants and metabolites in blood and adipose tissues of polar bears (*Ursus maritimus*) from Svalbard. SPFO Report 915/2004 , October 2004.
[20] Hobbs, K.E *et al.* Levels and patterns of persistent organochlorines in minke whale (*Balaenoptera acutorostrata*) stocks from the North Atlantic and European Arctic. Environmental Pollution 121 (2), 239-252, (2003).
[21] Gabrielsen G.W. *et al.* Organic Pollutants in Northern Fulmars (*Fulmarius glacialis*) from Bjørnøya. SPFO-Report 922/2005, January 2005
[22] N. Vulykh, *et al.* Model assessment of potential for long-range transboundary atmospheric transport and persistence of Endosulfan. EMEP Meteorological Synthesizing Centre East , Note 10/2005 (2005).

endosulfan and its formulated end-products to aqueous organisms, in particular to aqueous vertebrates[23].

Recent literature has indicated the potential for endosulfan to cause some endocrine disruption in both terrestrial and aquatic species. Effects observed were impaired development in amphibians, reduced cortisol secretion in fish, impaired development of the genital tract in birds and hormone levels, testicular atrophy and reduced sperm production in mammals resulting from endosulfan exposure.

Excessive and improper application and handling of endosulfan have been linked to congenital physical disorders, mental retardations and deaths in farm workers and villagers in developing countries in Africa, southern Asia and Latin America. Endosulfan was found among the most frequently reported intoxication incidents, adding unintentionally further evidence to its high toxicity for humans[24].

In laboratory animals, endosulfan produces neurotoxicity effects, which are believed to result from over-stimulation of the central nervous system. It can also cause haematological effects and nephrotoxicity. The α-isomer was generally found more toxic than the β-isomer[25].

Investigation of chronic human toxicity exert endosulfan to be neither a carcinogen nor a reproductive toxin nor a teratogen in mammals. There are several results *in vitro* and *in vivo* showing no mutagenic effect.

6 Statement of the reasons for concern

According to the available data, endosulfan is very persistent in the environment and is frequently found in environmental compartments. It has a great potential for bioaccumulation. Due to its physical and chemical properties and atmospheric half-life, and based on modelling data and findings in environmental samples, it has been proved that endosulfan is transported long distances, far from its sources. Endosulfan is a very toxic chemical for nearly all kind of organisms. Endosulfan has the potential to cause some endocrine disruption in both terrestrial and aquatic species. Endosulfan causes neurotoxicity and haematological effects and nephrotoxicity.

Placing on the market and use of endosulfan has been prohibited in the European Union. However, it is still produced in some countries (Worldwide production estimated at 10,000 metric tonnes.) and it continues to be used in many countries. Given the inherent properties of endosulfan, together with demonstrated or potential environmental concentrations that exceed maximum permissible concentrations; and given the widespread occurrence of endosulfan, including in remote areas; it is concluded that endosulfan is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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[23] US Environmental Protection Agency. ECOTOX data base. http://www.epa.gov/ecotox/.

[24] End of the Road for Endosulfan. Environmental Justice Foundation (2002). http://www.ejfoundation.org/pdfs/end_of_the_road.pdf

[25] ATSDR (Agency for Toxic Substances and Disease Register). Toxicological Profile for Endosulfan, September 2000. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp41.pdf