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Listing of chemicals in Annex III to the Rotterdam Convention: consideration of the draft decision guidance document for endosulfan

Consideration of the draft decision guidance document for endosulfan: tabular summary of comments

Note by the Secretariat

1. In accordance with the process for the development of decision guidance documents set out in decision RC-2/2, the internal proposal for endosulfan was circulated to the Chemical Review Committee and its observers for their information and comments. The annex to the present note contains a tabular summary of the comments received thereon and how they were taken into account in preparing the draft decision guidance document on endosulfan. The summary has not been formally edited.

2. The draft decision guidance document for endosulfan has been made available as document UNEP/FAO/RC/CRC.6/11.

* UNEP/FAO/RC/CRC.6/1.

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Annex

Tabular summary of comments on the internal proposal on endosulfan

Country	Section	Comment/Suggestion	Response
Australia	p.2 Purpose of DGD	Addition of: For example, the Stockholm Convention's draft risk profile on endosulfan was published after the notifying Parties provided the original information reproduced in this DGD. The draft risk profile provides new interpretations on data relating to persistence and bioaccumulation.	Addition not accepted because the draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it would be an option to consider the final outcome.
Chile	Abbreviations list	Suggestion to add the abbreviations "CSP, CILSS, IPM, ICSC, APVMA, NRA, AMAP, BCF, CT, DT, PEC, PIRI" to the list 2 minor editorial comments	Accepted and list amended, except for few abbreviations that were mentioned only once in the DGD Accepted
Crop Life (MAI)	Section 2.2	**Human health:** Based on the official minutes of the tripartite meeting (May 2004), the rapporteur and a representative of the Commission stated *"Rapporteur identified a safe use for operation. RMS considered the rest of the points in toxicology fulfilled"*. At that time, it was concluded that endosulfan is safe for operators and that the requirements in the area of toxicology according to 91/414 were fulfilled. The reference of the working group legislation to insufficient data regarding the operator risk is inaccurate, arbitrary, and not justified based on the available information.	The text in the draft DGD reflects the review report for the active substance endosulfan, which summarises the final conclusions of the risk assessment obtained by a peer review process. The review report was adopted by the Standing Committee on the Food Chain and Animal Health in support of the regulatory decision on endosulfan. Any disagreement with the review report should be submitted to the appropriate administration and not be raised in the CRC.
	Annex 1, Section 2	MAI agrees concerning the toxicological property of endosulfan, stating that endosulfan does not bioaccumulate, is not an endocrine disrupter or immunotoxicant, not a mutagen or carcinogen, and not a reproductive toxicant. The WHO classified endosulfan as moderately hazardous	Noted.
	Annex 1, Section 3.1	Food: We agree that dietary assessments (acute, chronic) for endosulfan are acceptable.	Noted
	Annex 1, Section 3.2	No further comment.	Noted
	Annex 1, Section 3.3	No further comment.	Noted
	Annex 1, Section 3.4	**Occupational Exposure –E.C. Assessment:** Using sound science-based input parameters that differ from those developed and used by the E.C. result in lower risks to Mixer/ Loaders and Applicators. Specifically, the use and	The text in the draft DGD reflects the report on the risk assessment for the active substance endosulfan. The report is the result of the risk assessment carried out by one Member State of the European Community, which was

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		mischaracterization of the nature and severity of toxicological endpoints (dermal vs. inhalation) to generate the total systemic Acceptable Operator Exposure Level (AOEL) combining the inhalation and dermal route of exposure is unacceptable. Before dermal and inhalation exposure can be aggregated for occupational risk, it is essential that the toxicological endpoint for each route of exposure must be the same and the route-specific doses must have a common mechanism of toxicity. The endpoints from the 1-year dog study (Brunk 1989) and repeat dose inhalation study (Hollander and Weigand 1984) are distinct and should not be combined when calculating the AOEL. This summation of risk is not appropriate for endosulfan's occupational risk assessment. In addition, a dermal penetration factor of 20 % is excessive. In view of the existing data base it should be less than 14% and can be as low as 2 %. Taking all of this into consideration would result in acceptable AOELs (<100 %)	peer reviewed by all other Member States. Any disagreement with the risk assessment should be submitted to the appropriate administration and not be raised in the CRC.
E.C.	Abbreviations	EC for European Commission E.C. for European Community	Added / amended as suggested in the whole document
	Section 1 Identification	Harmonized System Customs Code 2920 90 Other numbers: E.C. customs code: 2920 90 85	Amended as suggested
	Section 2.1.	For certain essential uses, under specific conditions, in specific Member States (listed in the Annex to the Commission Decision 2005/864/EC) a prolonged period of withdrawal of existing authorisations was allowed until 30 June 2007 under specific conditions. The period of grace for use of existing stocks expired on 2 June 2007 and for essential uses on 31 December 2007.	Wording amended / Sentence added as suggested
	Section 2.2.	*European* Commission	*European* added
	Section 3.1.	<u>DGD proposal</u> (E.C.) The ban of endosulfan as an active ingredient in plant protection products is expected to reduce significantly the input of endosulfan into the aquatic environment. All the applications as plant protection products, except the essential uses listed below, had been prohibited by the regulatory action. <u>New proposal</u> The ban of endosulfan as an active ingredient in plant protection products reduces the exposure of operators and the environment, including the aquatic environment and non-target organisms to this chemical.	New wording accepted

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		All uses as plant protection products had been prohibited by the regulatory action, including the essential uses listed below, for which the prohibition was delayed. DGD proposal (African countries) ... The phase-out that included a stepwise approach in order to avoid creating stockpiles led to a complete reduction of the risks to human health and the aquatic environment. New proposal ... The phase-out that included a stepwise approach in order to avoid creating stockpiles led to *an abolition of exposure, thus reducing the risks to human health and the aquatic environment.*	New wording not accepted. The former wording is preferred.
	Section 4.1.	DGD proposal Classification is (Commission Directive 2004/73/EC) **T** (Toxic) **Xi** (Irritant) **N** (Dangerous for the environment) Risk phrases: **R24/25** (Toxic in contact with skin and if swallowed) **R36** (Irritating to eyes) New proposal Classification in accordance with Council Directive 67/548/EEC: **T+** (Very Toxic) **Xn** (Harmful) **N** (Dangerous for the environment) Risk phrases: **R26/28** (Very toxic by inhalation and if swallowed) **R21** (Harmful in contact with skin)	New wording accepted. Explanation: The classification given before has not been up-to-date.
	Annex 1, Section 2.2.1	DGD proposal Endosulfan is classified as not irritating to the skin and eyes according to EU criteria. New proposal Endosulfan is classified as harmful in contact with skin and not irritating to eyes according to E.C. criteria.	New wording accepted
	Annex 1, Section 2.2.7	Comment: The last sentence contradicts information provided under 2.2.5, where effects on reproductive performance are reported.	Comment not fully agreed. Effects reported under 2.2.5 were moreover clinical signs and secondary effects (except for rat teratology study). Text was amended to “No clear effects…”
		Comment: the values for chronic RfD and drinking water as reported in section 4.2 should also be included here.	Values have been added as suggested
	Annex 1, Section 3.4	The following scenarios were accepted *for establishing* the final endpoints of the European Community risk evaluation based on the use of Thiodan EC 35	New wording accepted

Country	Section	Comment/Suggestion	Response
	Annex 1, Section 5.3	endosulfan poses a *high* risk to honey bees.	Accepted
	Annex 2 – 3	Unacceptable risk to non-target organisms (*fish*, birds and mammals, bees and earthworms).	Addition of `fish`accepted
	Annex 2 – 4.1	DGD proposal Reduction of risk from plant protection products. New proposal During the evaluation of endosulfan a number of areas of concern have been identified. The review concluded that exposure of operators under indoor conditions was not sufficiently addressed with the available information. In addition uncertainty concerning the formation of degradation products of endosulfan in the environment remained and risks to non-target organisms (fish, birds and mammals, bees and earthworms) were considered unacceptable	New wording accepted
	Annex 4	"European Commission" instead of "EU"	Accepted
Germany	IUPAC, CAS name	The IUPAC name is 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxa-thiepin-3-oxide. The CAS name is 6,9-methano-2,4,3-benzodioxathiepin, 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-3-oxide	Noted.
	Annex 1, Section 2.1	Discrepancy between the date indicated for the meeting of the Sahelian Pesticide Committee in the annex to the notification - May 8th, 2007 - and the date of the meeting as 24 - 26 July 2006 in the notifications of the Sahel States	The date in the official document is May 8th.
	Annex 1, Section 2.2.1 and 2.2.7	According to the Preliminary Risk and Value Assessments of Endosulfan REV2007-13 from PRMA Health Canada (2007), endosulfan is highly acutely toxic via the oral and inhalation routes in rats. It was also highly toxic via the dermal route in rabbits. Replacing of "low acute dermal toxicity" to "highly toxic via the dermal route in rabbits" is suggested. Information from the draft risk profile on endosulfan (Stockholm Convention) stating that Endosulfan is a slight eye and skin irritant in rabbits should be included.	High acute and inhalation toxicity is already mentioned. Furthermore, the PMRA Assessment is not an information source for the DGD. The draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.
	Annex 1, Section 4.1.1	The high persistency (much more than the parent compounds and about the same toxicity) of the main metabolite endosulfan sulfate should be mentioned. The draft risk profile on endosulfan (Stockholm Convention) states from the E.C. risk assessment that the DT50 for aerobic soil	The draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.

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		degradation for endosulfan sulfate ranges from 123 -391 days under laboratory conditions. It is also important to mention that all the metabolites maintain the chlorinated cyclic structure of endosulfan which indicates a potential for persistency and bioaccumulation.	
	Annex 1, Section 4.1.3	It should be mentioned, that endosulfan and its metabolites undergo long range atmospheric transport (LRAT) and can be found in the arctic biota.	This information is from the draft POPRC risk profile (2009). See response above.
	Annex 1, Section 4.1.4	It is not clear, from which species this data is derived and so this information should be added. In the Preliminary Risk and Value Assessments of Endosulfan REV2007-13 depuration half-lives of 2.9 - 5.9 days are reported for zebra fish.	It is not clear, to which data the question on species is related.
	Annex 1, Section 4.1.5	The last sentence seems to be contradicting, because in 4.1.2 a half-live of >200 days under acidic conditions was mentioned and there are many water bodies in the northern hemisphere which are quite acidic nowadays due to acidification processes (e.g. acid rain). The last sentence should be altered to reflect the persistency of endosulfan under acidic conditions.	The text has been amended as suggested.
Nigeria		No comments	Noted
Norway	Annex 1	These results do not differ substantially from the information provided by the notifying countries, but the AMAP report *provides* additional data on the environmental fate in air and the potential for bioconcentration/bioaccumulation (Sections 4.1.3 and 4.1.4).	`does provide`changed to `provides` as suggested
	Annex 1, Section 4.1.4	the real risk of biomagnification is *assumed* to be lower	New wording accepted
	Annex 4	Persistent Organic Pollutants in the Arctic - Chapter 4B: Regional and Circumpolar Levels and Trends in Abiotic and Biotic Media.	more detailed reference added as suggested
PAN	Manufacturers	Additional maunufacturer`s names provided	The maunufacturer`s names provided were added to the list; former manufacturers were kept
	Section 3.3.	General Countries should consider promoting, as appropriate, integrated pest management (IPM) *and organic* strategies as a means of reducing or eliminating the use of hazardous pesticides. Advice may be available through National IPM focal points, the FAO, *IFOAM (International Federation of Organic Movements)*, and agricultural research or development agencies.	Amendmends accepted

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	Annex 1, Section 2.1.3	In humans it is widely found in breast milk (Cerillo et al 2005). See PANAP monograph	The PANAP monograph is not an information source for the DGD
	Annex 1, Section 2.2.2	inhalation NOAEL of 0.001 mg/l from EPA assessment should be reported	NOAEL added
		pregnant rabbit 12-days NOAEL of 0.7 mg/kg/bw to be mentioned	NOAEL not added, because it is not found in the information sources of the DGD
	Annex 1, section 2.2.3	DGD proposal Endosulfan gave the following results in genotoxicity tests: did not induce gene mutation in bacterial or mammalian cells; it appears to be non-mutagenic for yeast (however, the conduct of these studies is questionable); it was not clastogenic in cultured human lymphocytes following acute exposure (however, effects of chronic exposure or in the presence of metabolic activation were not assessed); it did not induce DNA damage in bacteria (rec-assay) or in cultured mammalian cells (UDS) (however, the conduct of these studies is questionable); it is non-clastogenic in mammalian somatic cells *in vivo*; it induced sperm abnormalities in rodents (E.C., 2005). New proposal The assessments conducted by the EU, Canada or the USA considered that endosulfan is not carcinogenic. However, Bajpayee et al., (2006) found that exposure to sublethal doses of endosulfan and its metabolites induce DNA damage and mutation. Although the contribution of the metabolites to the genotoxicity of the parent compound in Salmonella and mammalian cells was unclear, and the pathways leading to bacterial mutation and mammalian cell DNA damage appeared to differ (draft POPRC risk profile, 2009).	The draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.
	Annex 1, Section 2.2.6	DGD proposal Endosulfan is not classified as being either an endocrine disruptor or an immunotoxicant. New proposal There are contradictory opinions on whether endosulfan is an endocrine disruptor. Recent information indicates that endosulfan mimics non-utertrophic E(2) actions, strengthening the hypothesis that endosulfan is a widespread xenoestrogen, acts via a membrane version of the estrogen receptor-*a* on pituitary cells and can provoke CA^{++} influx via L-type channels, leading to prolactin (RL) secretion, and is also anti-progestative (draft POPRC risk profile, 2009).	The draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.

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	Annex 1, Section 2.2.7	Endosulfan is genotoxic *in some studies, but carcinogenic effects were not observed* in studies on mice and rats.	The draft POPRC risk profile (2009) is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.
	Annex 1, Section 3.1	Addition of: However, residues in food are widespread and thought to be the main cause of endosulfan residues in humans (Campoy et al 2001)	New sentence not accepted, because it is not found in the information sources of the DGD.
	Annex 1, Section 3.3	The US EPA (2007) considers that the contribution from residues in drinking water is the major dietary risk contributor	Not added, because it is not found in the information sources of the DGD.
	Annex 1, Section 3.4	Reported occupational exposure: Addition of: An agricultural pilot exposed to endosulfan showed persistent "nonspecific epileptic foci in the cerebral frontal lobes" (ATSDR 2000).	Not added, because it is not found in the information sources of the DGD.
		A range of surveys carried out by PAN Africa in Senegal, in 2003-2004, mainly in cotton growing areas of the Velinagar region, identified endosulfan as the cause in 31.2 to 39.9% of cases of poisoning. Of all the 162 poisonings, including 20 deaths, 73.2% occurred from exposure during application (Glin et al 2006).	Not added, because it is not found in the information sources of the DGD
		In Bénin, 37 people (producers and others) died between May and September 1999, while 36 others suffered severe poisonings from Callisulfan (endosulfan 350 g) in the Borgou department, according to the Regional Action Centre for Borgou Rural Development. These poisonings were either direct (while using endosulfan, mainly while treating cotton plants) or indirect (after consumption of contaminated food, mainly vegetables) (PAN & IPEN 2009)	Not added, because it is not found in the information sources of the DGD
	Annex 1, Section 4.1.4	Addition of: Endosulfan also has a log Koa of 10.29 which indicates a high potential to bioccumulate in air-breathing organisms resulting in biomagnification in the terrestrial food chain (Kelly & Gobas 2003; Kelly et al 2007).	This information is from the POPRC risk profile (2009). The draft POPRC risk profile is still under discussion and not yet finalised. After finalisation it is an option to consider the final report.
		DGD proposal The BCF (bioconcentration factor) is between 2500 and 11583 and with a log Kow of 4.7, this indicates a high potential to bioaccumulate. However, the clearance is very rapid (CT_{50} = 2 days), so the real risk of biomagnification is assumed to be lower. New proposal However, the clearance is very rapid (CT_{50} = 2 days, CT = clearance time), so the real risk of biomagnification is assumed to be lower in aquatic food chains and higher in terrestrial food chains. Model estimations, based on	see above

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		measured concentration of key elements from remote Arctic food chains, indicates a significant biomagnification of endosulfan in terrestrial ecosystems (POP draft risk profile, 2009).	
	Annex 1, Section 4.1.5	Addition of: The estimated half-lives for the combined toxic residues (endosulfan plus endosulfan sulfate) ranged from roughly 9 months to 6 years. (US EPA, 2002. Reregistration Eligibility Decision).	Text added as suggested
	Annex 1, Section 4.2.5	Addition of: Endosulfan treatment of cotton fields in India resulted in a 60.5% decrease in the population of actinomycetes 10 days after treatment (Vig et al 2008). Endosulfan is also toxic to the major groups of beneficial small soil invertebrates, mites and springtails, causing a persistent decline in populations. These invertebrates are key to maintaining soil fertility and mixing the organic and mineral components of soil (Joy & Chakravorty 1991).	Not added, because it is not found in the information sources of the DGD
	Annex 1, Section 5.5	Addition of: It is however expected to cause effects on the humic content of the soil, because of its effects on the major groups of beneficial small soil invertebrates, mites and springtails, which are are key to maintaining soil fertility and mixing the organic and mineral components of soil (Joy & Chakravorty 1991).	Not added, because it is not found in the information sources of the DGD
Switzerland	Abbreviations list	DT_{50} resp. DT_{90} (disappearance time for 50 % resp. 90 % of the initial residues) to be mentioned in the list of abbreviations	"DT" has been added to the list
Turkey		No comments	Noted