

## **COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT**

**First draft statement on endosulfan isomers, pentachlorobenzene and chlordecone in relation to infant diet.**

### **Introduction**

1. The Committee on Toxicity (COT) has been asked to consider the toxicity of chemicals in the infant diet, in support of a review by the Scientific Advisory Committee on Nutrition (SACN) of Government recommendations on complementary and young child feeding. An initial paper (TOX/2012/03), highlighting some of the areas for possible consideration was discussed by the COT in February, 2012, and Members concluded that number of persistent organic pollutants (POPs) included in the Stockholm convention since 2009 required further evaluation. A brief overview of the toxicology and occurrence data available for endosulfan and its related isomers, and for pentachlorobenzene and chlordecone (TOX/2013/15) was presented to Members in March 2013.

2. Annex A contains the first draft COT statement summarising the available information and the Committee's provisional conclusions on endosulfan, pentachlorobenzene and chlordecone.

3. This first draft statement responds to the discussion of the overview in March 2013. Additional searches for more recent toxicity studies and data on residues, such as in breast milk, have been included where available. Additional searches excluded studies performed in plants and freshwater organisms, studies related to occupational exposure or levels of POPs in soil, freshwater and wastewater samples. Information on residue data available from the UK and European studies has been considered more relevant.

### **Questions on which the views of the Committee are sought**

4. Members are invited to comment on the structure and text of the draft statement.

**Secretariat  
April 2013**



## COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

### First draft statement on endosulfan isomers, pentachlorobenzene and chlordecone in relation to infant diet.

#### Background

1. The SACN is undertaking a review of scientific evidence that bears on the Government's dietary recommendations for infants and young children. The review will identify new evidence that has emerged since the Government's current recommendations were formulated, and will appraise that evidence to determine whether the advice should be revised. The recommendations cover diet from birth to age five years, but will be considered in two stages focussing first on infants aged 0-12 months, and then on advice for children aged 1 to 5 years. SACN is examining the nutritional basis of the advice, and has asked that evidence on possible adverse effects of diet should be considered by other advisory committees with relevant expertise. In particular, SACN asked COT to review the risks of toxicity from chemicals in the infant diet.

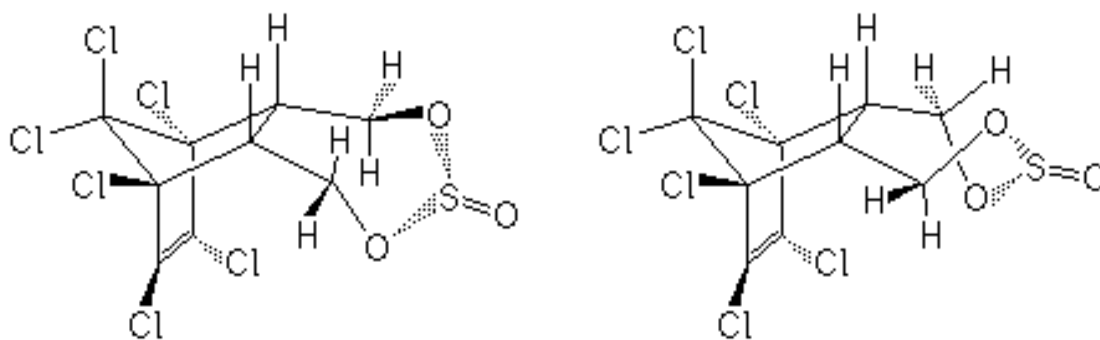
2. The COT considered that chemicals recently classed as persistent organic pollutants (POPs) under the Stockholm Convention should be included in this series of evaluations as such substances have the potential to accumulate in the food chain. This statement provides information on the available occurrence and exposure data and potential risks from selected POPs: endosulfan isomers, pentachlorobenzene and chlordecone in the infant diet. A summary of the background and the main toxicological properties for each chemical have been included to provide an overview of the similarities and differences in relation to their toxicity as well as to the toxicological information available.

#### Endosulfan

3. Endosulfan occurs as two biologically active isomers:  $\alpha$ - and  $\beta$ -endosulfan (Figure 1). Technical endosulfan is a mixture of the two isomers along with small amounts of impurities and degradation products (UNEP, 2011).

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**Figure 1.** Structures of endosulfan isomers.



4. Endosulfan is an insecticide that had been used since the 1950s to control crop pests, tsetse flies and ectoparasites of cattle and as a wood preservative. As a broad-spectrum insecticide, endosulfan is currently used to control a wide range of pests on a variety of crops including coffee, cotton, rice, sorghum and soy in some parts of the world. Endosulfan has not been authorised as a pesticide in the European Union since 2005 due to concerns about environmental fate, ecotoxicological profile and the risk to operators during application and is now regulated as an undesirable substance in animal feed (EFSA, 2011). Endosulfan was included in the list of new POPs in the Stockholm Convention in 2011 since it meets the criteria for long-range transport, bioaccumulation, persistency in the environment and toxicity. Currently, the use of endosulfan is banned or will be phased out in 60 countries that, together, account for 45 per cent of current global use (UNEP, 2011).

5. Technical endosulfan and its isomers have not been evaluated by the COT or its sister committees on Mutagenicity (COM) or Carcinogenicity (COC), or by the International Agency for Research on Cancer (IARC). It has been evaluated by European Food Safety Authority (EFSA) as an undesirable substance in animal feed (EFSA, 2005), which did not include establishment of health-based guidance values. The latest evaluation of endosulfan undertaken by the Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Meeting on Pesticide Residues (JMPR) was in 1998 (FAO/WHO, 1998). The International Programme on Chemical Safety (IPCS) of the WHO also evaluated endosulfan in the Environmental Health Criteria series in 1984 (WHO-IPCS, 1984) and in the Health and Safety Guide in 1988 (WHO-IPCS, 1988). In the US, endosulfan was evaluated by the Agency for Toxic Substances and Disease Registry (ATSDR) in 2000 and the Environmental Protection Agency (EPA) in 2002. This statement draws on the information in these authoritative reviews supplemented by more recent relevant scientific publications where available.

### Toxicokinetics

6. Endosulfan is readily absorbed from the gastrointestinal tract in experimental animals and humans, with differing distribution patterns of the isomers.

7. No information is available on the metabolism of endosulfan in humans. In rodents, it is metabolised to endosulfan sulphate and endosulfan diol, which can be

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further metabolised to endosulfan lactone, hydroxyether and ether (WHO-IPCS, 1984; FAO/WHO, 1998).

8. Renal excretion is the most important elimination route in humans and animals. Biliary excretion has also been demonstrated to be important in animals. Estimated elimination half-lives ranged between approximately 1 and 7 days in adult humans and animals e.g. male rats showed a biphasic curve with an initial half-life of 8 hours followed by a half-life of 110 hours (FAO/WHO, 1998; ATSDR, 2000). Endosulfan can be transported across the placenta (Schaalan *et al.*, 2012) and transferred into the breast milk in lactating women and animals (ATSDR, 2000; Schaalan *et al.*, 2012).

## Toxicity

9. Neurotoxicity was shown to be the most prominent effect of endosulfan exposure. Other effects include liver and kidney toxicity (FAO/WHO, 1998; Choudhary *et al.*, 2003). Some studies indicate effects on the immune system but no adverse effects on organs of the immune system were reported following chronic studies (ATSDR, 2000).

10. A number of studies indicate endosulfan has no adverse effects on reproductive performance in animals; however, adverse effects on male reproductive organs such as reduced sperm count or increased testis weight have been seen in young rats and mice (FAO/WHO, 1998; ATSDR, 2000; Sinha *et al.*, 2001).

11. JMPR concluded that endosulfan was not genotoxic in an adequate battery of tests for mutagenicity and clastogenicity *in vitro* and *in vivo*, which included bacterial mutation assays in *Salmonella typhimurium* and *Escherichia coli*, the mouse lymphoma assay, chromosome aberrations in human lymphocytes and rat bone marrow, and dominant lethal mutation in mice (FAO/WHO, 1998). Subsequently, a number of studies have indicated that endosulfan can cause DNA damage, possibly by a mode of action involving reactive oxygen species (Antherieu *et al.*, 2007; Ahmed *et al.*, 2008; Ahmed *et al.*, 2011; Bajpayee *et al.*, 2006; Jamil *et al.*, 2004; Lu *et al.*, 2000; Li *et al.*, 2011). Recent data have also shown evidence of mutagenicity in the Ames test (Bajpayee *et al.*, 2006; Yaduvanshi *et al.*, 2012). Bajpayee *et al.* reported that endosulfan produced positive responses (two fold the background) in *Salmonella* strains TA100 and TA102 at concentrations of 1-20 µg/plate. In comparison, endosulfan isomers and its metabolites produced the highest positive responses (three-fold the background) in TA97a and TA98 strains, and in TA100 and TA102 strains (endosulfan diol only). The maximum response was observed for all compounds (with and without metabolic activation) at 10 µg/plate with a subsequent decrease at 20 µg/plate (Bajpayee *et al.*, 2006). The concentrations used in this study were 250 times lower than those reported to be negative in studies summarised by JMPR (FAO/WHO, 1998). Contradictory results were obtained by Yaduvanshi *et al.*, who reported multiple-fold increase in colonies only in TA98 strain at 500 µg endosulfan/plate and in absence of metabolic activation (Yaduvanshi *et al.*, 2012). Overall, the evidence for direct mutagenicity of endosulfan is inconsistent.

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12. Chronic feeding studies with endosulfan in rats and mice did not produce carcinogenic effects (FAO/WHO, 1998).

13. Contradictory results have been reported on oestrogenic potential of endosulfan *in vitro* whereas generally negative outcomes have been obtained *in vivo* (ATSDR, 2000; Ozen *et al.*, 2012). Some subsequent animal studies suggested that endosulfan can mimic non-uterotropic oestrogenic actions (Varayoud *et al.*, 2008).

14. The information on effects of endosulfan in humans mostly relates to accidental, intentional or occupational exposure. In the case of occupational exposure, it is generally not possible to ascribe effects exclusively to endosulfan in environments with a mixture of chemicals which limits the interpretation of such studies for the purposes of risk assessment. Human data have not shown evidence of carcinogenicity for endosulfan (ATSDR, 2000). Exposure to endosulfan has been linked to congenital physical disorders, mental retardations and deaths in farm workers and villagers in developing countries in Africa, Asia and Latin America (EFSA, 2005). In a recent study advanced sexual development (including breast enlargement and menstruation) in 4 month old girl was suggested to be caused by pesticide contamination of her family farm (Gaspari *et al.*, 2011).

### **Health-based guidance values**

15. JMPR (FAO/WHO, 1998) established an acceptable daily intake (ADI) of 0.006 mg/kg b.w. for endosulfan on the basis of the no-observed adverse effect level (NOAEL) of 0.6 mg/kg b.w./day in the two-year dietary study of toxicity in rats and a safety factor of 100. Reduced body weights and pathological findings in the kidney and lymph nodes were observed at higher doses. The ADI was supported by similar NOAEL values in the 78-week dietary study of toxicity in mice (NOAEL of 0.58 mg/kg b.w./day), a one-year dietary study of toxicity in dogs (NOAEL of 0.8 mg/kg b.w./day), and a study of developmental toxicity in rats (NOAEL of 1.5 mg/kg b.w./day). An acute reference dose (ARfD) of 0.02 mg/kg bw/day was established on the basis of the NOAEL of 2 mg/kg bw /day in a study of neurotoxicity in rats with a safety factor of 100. Although some mutagenicity of endosulfan was shown in subsequently published studies, the lack of consistency in the reported effects, together with the lack of carcinogenicity, do not provide convincing evidence that the ADI and ARfD are inappropriate.

### **Occurrence in food and breastmilk**

16. A survey of pesticide residues in animal feed ingredients was conducted in the UK in 1998, in which samples of cereals, fodder and beans were analyzed for 28 different pesticides including endosulfan. None of these samples contained endosulfan at concentrations over the detection limit (50 µg/kg) (MAFF-UK, 1998).

17. In the UK Pesticide Residues Monitoring Programme in 2009 and 2011 there were no reports of infant foods containing endosulfan at or above the maximum residue level (MRL) of 0.01 mg/kg. The analysed foods were infant food (meat/fish/egg/cheese), cereals fruit and vegetables (PRiF, 2009, 2011).

18. Shen *et al.* (2008) detected  $\alpha$ -endosulfan in all breastmilk samples obtained between 1997 and 2001 of Finnish (4-8 weeks postpartum; n=65) and Danish (4-12 weeks postpartum; n=65) women, with median (range; LOD) concentrations of 6.40 (1.19 – 22.66; LOD 0.01-0.38) and 7.43 (1.92 – 18.05; LOD 0.01-0.31)  $\mu\text{g}/\text{kg}$  lipid, respectively. Levels of  $\beta$ -endosulfan were reported as undetectable. The respective median lipid content was 4.26 and 2.84 % w/w. Therefore, it can be estimated that median levels of  $\alpha$ -endosulfan in the Finnish and Danish samples were approximately 0.27 and 0.21  $\mu\text{g}/\text{L}$  breastmilk, respectively. In Spain all of 23 breastmilk samples collected between 2000 and 2002<sup>1</sup> (2-5 weeks postpartum,) contained endosulfan isomers:  $\alpha$ -endosulfan was detected with a median value of 0.87 (max 1.00) and  $\beta$ -endosulfan: 7.29 (max 26.89)  $\mu\text{g}/\text{L}$  breastmilk (Cerrillo *et al.*, 2005).

## Exposure

19. No data on exposure to endosulfan in the UK population have been identified. Exposures were estimated in Canada in a location with maximum intake (0.03  $\mu\text{g}/\text{kg}$  b.w./day, 5-11 years old maximum exposure age group), the USA (0.05  $\mu\text{g}/\text{kg}$  b.w./day), Taiwan (0.01  $\mu\text{g}/\text{kg}$  b.w.) and the Czech Republic (0.015  $\mu\text{g}/\text{kg}$  b.w./day) based on occurrence data from the 90s (EFSA, 2005).

20. The reported minimum (0.21  $\mu\text{g}/\text{L}$  breastmilk as  $\alpha$ -endosulfan, estimated based on Shen *et al.*, 2008) and maximum (8.16  $\mu\text{g}/\text{L}$  breastmilk as a sum of  $\alpha$ - and  $\beta$ -endosulfan, as reported by Cerrillo *et al.*, 2005) concentrations of endosulfan in breastmilk in the EU (have been used to estimate potential exposure of breastfed infants. with average (800 mL per day) and high level (1200 mL per day) consumption (Table 1). The bodyweight data from the recently published UK Dietary and Nutrition Survey of Infants and Young Children (DNSIYC) (DH, 2013), with an average of 7.8 kg for infants aged 4 – 6 months, were used to calculate potential intakes for this age group. Since DNSIYC did not include infants younger than 4 months, in this statement the value of 5.9 kg for infants aged 0 – 3 months (DH, 1994), is applied to infants aged 0 – 4 months. The estimated intakes are in the range of 0.02 – 1.11  $\mu\text{g}/\text{kg}$  bw/day for average consumption and 0.03 – 1.66  $\mu\text{g}/\text{kg}$  bw/day for high level consumption. These are all considerably below the ADI of 20  $\mu\text{g}/\text{kg}$  bw/day set by JMPR in 1998. No data are available to allow estimation of possible dietary exposure from other sources.

**Table 1. Endosulfan exposure ( $\mu\text{g}/\text{kg}$  bw/day) from exclusive breastfeeding estimated for average and high level consumption**

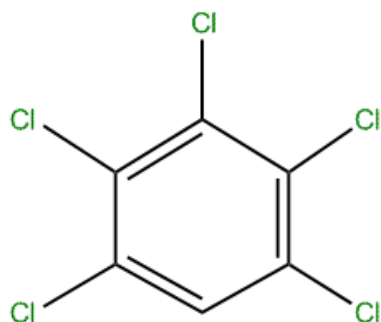
Endosulfan concentration in breastmilk*	Age in months (consumption volume)			
	0 – 4 (800 mL)	0 – 4 (1200 mL)	>4 – 6 (800 mL)	>4 – 6 (1200 mL)
Mean: 0.21 $\mu\text{g}/\text{L}$	0.03	0.04	0.02	0.03
Maximum: 8.16 $\mu\text{g}/\text{L}$	1.11	1.66	0.83	1.25

<sup>1</sup> Information on sampling time was provided in personal communication from the author

## **Pentachlorobenzene**

21. Pentachlorobenzene (PeCB) was used as a flame retardant and in dyestuff carriers. PeCB can still be found at low levels as an impurity in several herbicides, pesticides and fungicides. The main sources of PeCB nowadays include combustion of solid wastes, biomass burning, and degradation of the agricultural fungicide, quintozene. It is also still present in the atmosphere, sediments and biota (Bailey *et al.*, 2009).

**Figure 2.** Structure of pentachlorobenzene.



22. PeCB has not been evaluated by the COT, COM, COC, EFSA or IARC. It has been evaluated in the context of “chlorobenzenes other than hexachlorobenzenes” by the IPCS (WHO-IPCS, 1991). Other evaluations have been carried out by US EPA (EPA) (1998) and United Nations Environment Program (UNEP) (2007). This statement draws on the information in these authoritative reviews supplemented by more recent relevant scientific publications where available.

23. JMPR has not evaluated PeCB on its own. However, PeCB was used as a chemical intermediate in the production of quintozene, a fungicide evaluated in 1998, whose toxicity is partly due to the presence of PeCB. Plant protection products of quintozene containing more than 10 g/kg PeCB were banned in the European Union in 1990. Currently, quintozene is manufactured by a different procedure that does not use PeCB (UNEP, 2007).

24. In 2009, the Stockholm convention agreed to eliminate the use of PeCB on the basis of persistence in the environment, bioaccumulation, long-range environmental transport, moderate and high toxicity in laboratory mammals and aquatic organisms respectively. Regulation (EC) No 850/2004 was subsequently amended in 2010 prohibiting the production, use and marketing of PeCB in the EU.

## **Toxicokinetics**

25. In studies in rats and coyotes PeCB was readily absorbed and distributed in blood, liver, kidney and adipose tissue of rats (Umegaki *et al.*, 1993; Johnston *et al.*, 1997). PeCB metabolites were detected in the faeces. In rats, PeCB in faeces



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amounted to 4.8 % of the original dose. In coyotes, PeCB residues and metabolites were detected 6 months after dosing.

26. Serum concentrations of PeCB measured in children at birth and at four years of age were shown to be correlated with the age of mother and subsequently breastfeeding and the age of lactation (Carrizo *et al.*, 2006), indicating that PeCB is accumulative in humans.

## Toxicity

27. In acute studies PeCB resulted in decreased activity and tremors in rodents at sub-lethal doses; the kidneys, liver and adrenal glands of rats were also enlarged (UNEP, 2007). Sub-chronic and chronic studies provided consistent findings at approximately 500 mg/kg with increased liver weight generally in conjunction with hypertrophy, increased kidney weight with occasional hyalinization, disruption of the thyroid function and increased weight of the adrenal glands. At higher doses (1000 mg/kg), the same effects, though more severe, were reported. There were modulations in blood parameters such as haemoglobin and white blood cells (UNEP, 2007).

28. The UNEP (2007) evaluation reported contrasting outcomes in reproductive toxicity studies. Fetotoxicity has been reported in rats at doses that were non toxic in mothers. In contrast, no embryotoxic, fetotoxic or teratogenic effects were observed in the offspring of mice at doses that were maternally toxic. The most reported no effect (NOAEL) and lowest effect levels (LOAEL) varied between 17 and 200 mg/kg PeCB per day.

29. PeCB does not appear to be genotoxic. It was negative in the Ames test, with and without activation, and tests for a variety of cytogenetic endpoints (Gustaffson *et al.*, 2000 cited in UNEP, 2007). Preneoplastic foci formation in rat liver has been described following diethylnitrosamine initiation (Thomas *et al.*, 1998; Ou *et al.*, 2001). In assessing the toxicity of PeCB, the US EPA (1998) and UNEP (2007) stated that there is a lack of data in humans in order to determine its carcinogenicity.

30. PeCB reduced IL-6 levels *in vitro* in lymphocytes from individuals with allergic disease, such as atopic asthma or dermatitis, and non-allergic donors in a similar manner indicating a lack of impact on allergic response (Devos *et al.*, 2004).

## Health-based guidance values

31. The US EPA established a reference dose (RfD) of 0.8 µg/kg bw/day based on a LOAEL for liver and kidney damage in a sub-chronic study by Linder *et al.*, (1980) with an uncertainty factor of 10,000 (US EPA, 1998). Health Canada established a TDI of 0.5 µg/kg bw/day based on a sub-chronic study with a LOAEL for hepatocellular hypertrophy and necrosis of 5.2 mg/kg bw/day and an uncertainty factor of 10,000 (NTP, 1991). No additional studies, indicating that those values should be amended, have been found.

## Occurrence in food and breastmilk

32. PeCB is not a pesticide and thus it is not included in the UK pesticide monitoring programme nor is it covered by the pesticides MRL. No relevant data on levels of PeCB in food products are available.

33. The FSA has approved an investigative survey of PeCB in food, which will include infant foods and formulae. The results are expected to be available in 2015.

34. Data on PeCB in human breast milk in the UK have not been identified. PeCB was detected in all breastmilk samples obtained between 1997 and 2001 in Finland (4-8 weeks postpartum; n=65) and Denmark (4-12 weeks postpartum; n=65) with median (range; LOD) concentrations of 0.25 (0.08 – 1.17; LOD  $\leq$ 0.01) and 0.32 (0.13 – 1.41; LOD  $\leq$ 0.02)  $\mu\text{g}/\text{kg}$  lipid, respectively. The respective median lipid content was 4.26 (Finnish samples) and 2.84 (Danish samples) % w/w (Shen *et al.*, 2008). Based on those values it can be estimated that the breastmilk contained approximately 0.01  $\mu\text{g}$  of PeCB/L.

## Exposure

35. No data on exposure to PeCB in the UK population have been identified

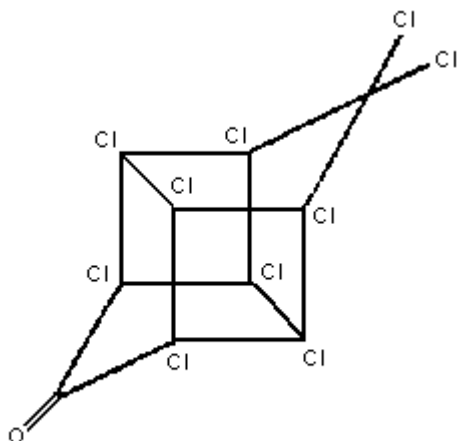
36. The concentration of PeCB in breastmilk estimated from the study by Shen *et al.*, 2008 (0.01  $\mu\text{g}/\text{L}$ ) was used to estimate potential PeCB exposure for average (800 mL) and high level (1200 mL) consumption by exclusively breastfed infants. The bodyweight and age criteria used were as described in paragraph 20. The estimated exposure is approximately 0.001  $\mu\text{g}/\text{kg}$  bw/day for average consumption and 0.002  $\mu\text{g}/\text{kg}$  bw/day for high level consumption. These are considerably below the TDI of 0.5  $\mu\text{g}/\text{kg}$  bw/day established by Health Canada (1993).

## Chlordecone

38. Chlordecone is a synthetic chlorinated organic compound used as an agricultural insecticide, miticide and fungicide. It was marketed as Kepone<sup>®</sup>. In the UK, all Kepone<sup>®</sup> and Kepone<sup>®</sup> derivatives had their licence for sale revoked in July 1977 (DEFRA, 2012). According to DEFRA, “Chlordecone may not have been used in the UK prior to its ban in 1977”.

**Figure 1.** Structure of chlordecone

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39. In 2009, the Stockholm convention agreed to eliminate chlordecone on the basis of persistence in the environment, bioaccumulation, long-range transport and toxic effects. UNEP considered there was extensive data from occupational exposure showing potential for adverse effects on humans including carcinogenicity and reproductive effects and very high toxicity for aquatic organisms (UNEP, 2007). In turn, Regulation (EC) No 850/2004 was updated in 2010 to prohibit the production, use and marketing of chlordecone in the EU.

40. Chlordecone has not been evaluated by the COT, COM, COC, EFSA or JMPR. A number of international bodies have published reports on chlordecone, such as IARC (1979, 1987), WHO-IPCS (1984 and 1990), ATSDR (1995), UNEP (2007) and US EPA (2009).

### Toxicokinetics

41. Chlordecone is well absorbed following oral, dermal and inhalation exposure. It is widely distributed in the body, with accumulation in the liver and to a lesser extent in fat, brain and kidneys, both in experimental animal studies and in humans (ATSDR, 1995; IPCS-WHO, 1984). Chlordecone is metabolised to chlordecone alcohol in some species, including humans. Elimination is mainly via the bile either as unmetabolised chlordecone or as the glucuronide conjugate of the alcohol (US EPA, 2009).

42. Workers occupationally exposed to chlordecone had high concentrations in the liver, whole blood and subcutaneous fat. The half-life was estimated to be 63 to 148 days and elimination was primarily in the faeces at a mean daily rate of 0.075% of the estimated total store in the body (US EPA, 2009).

### Toxicity

43. Chlordecone has been shown to cause neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animals. Liver cancer was induced in rats at a dose of 1 mg/kg bw/day (UNEP, 2007).

44. Chlordecone has been evaluated under the EU-Strategy for Endocrine Disrupters<sup>2</sup> and placed in category 1 (evidence of endocrine-disrupting activity in at least one species using intact animals). This categorisation was based on evidence of endocrine disruption activity in a number of experimental systems including the mouse uterotrophic assay, increased uterine weight in rats given multiple injections of chlordecone postnatally and receptor binding assays, indicative of an oestrogenic effect (BKH, 2000).

45. Chlordecone was not genotoxic in microbial and *in vitro* mammalian cell gene mutation assays, in a clastogenicity test and in the dominant lethal assay (ATSDR, 1995). It has been suggested that the hepatocarcinogenicity involves an epigenetic, tumour-promoting mechanism involving both hepatic toxicity and hypertrophy, and cytochrome P-450 induction (UNEP, 2006).

46. In humans, neurotoxicity has been reported in workers exposed to chlordecone during its manufacture (ATSDR, 1995). A number of studies reported oligospermia and decreased motility but not reduced fertility in occupationally exposed workers (Guzelian, 1982; Taylor, 1982, 1985). No evidence of hepatic cancer was found in liver biopsy samples taken from workers with hepatomegaly resulting from intermediate- or chronic-duration exposures to high concentrations of chlordecone (Guzelian *et al*, 1980). Environmental contamination of chlordecone in the French West Indies has been widely reported. This has led to a number of epidemiological studies in the affected area. In a recent study increasing plasma chlordecone concentration, resulting from exposure in adulthood over a 30-year period, was associated with increased risk of prostate cancer (Multigner *et al*, 2010).

## Occurrence

47. No data on chlordecone in human breastmilk in the UK have been identified.

48. Chlordecone has not been monitored in the UK Pesticide Residues Monitoring Programme. In 2010, EFSA presented results of the monitoring of pesticide residues in food and reported chlordecone to be tested in 5 European countries. However, it was found at quantifiable levels only in two samples (out of 9214) of fruit and vegetables (lower to upper confidence interval was 0.00 - 0.08) (EFSA, 2010).

## Exposure

49. No information has been identified on exposure to chlordecone from human breastmilk or the diet in the UK.

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<sup>2</sup> [http://europa.eu.int/comm/environment/endocrine/strategy/substances\\_en.htm](http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm)

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## **Conclusions**

50. Endosulfan has not been authorised as a pesticide in the European Union since 2005. Significant residues in food are not expected. Although there are some data on endosulfan in breastmilk samples in Europe, the potential dietary exposure of breastfed infants would be considerably lower than the ADI of 20 µg/kg bw/day set by JMPR in 1998.

51. No data on PeCB in food have been found. Reported levels of PeCB in breastmilk samples would result in exposure to infants considerably below the TDI of 0.5 µg/kg bw/day set by Health Canada.

52. There are no data available on chlordecone in food or human breastmilk. However, even if chlordecone has been previously used in the UK, the exposure would be expected to be decreasing.

53. The Committee concluded that, based on the available information, there appeared to be no toxicological concern about any of the three chemicals since exposures were below the ADI, or if no ADI had been set, were low and decreasing.

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## Abbreviations

ADI	acceptable daily intake
ARfD	acute reference dose
ATSDR	Agency for Toxic Substances and Disease Registry
COC	Committee on Carcinogenicity
COM	Committee on Mutagenicity
COT	Committee on Toxicity
DH	Department of Health
DNSIYC	Dietary and Nutrition Survey of Infants and Young Children
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
FAO/WHO	Food and Agriculture Organization/World Health Organization
FSA	Food Standards Agency
IARC	International Agency for Research on Cancer
IPCS	International Programme on Chemical Safety
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LOAEL	lowest observed adverse effect level
LOD	Limit of Detection
MAFF	Ministry of Agriculture, Forestry and Fisheries
MRL	maximum residue level
NOAEL	no-observed adverse effect level
NTP	National Toxicology Program
PeCB	pentachlorobenzene
POPs	persistent organic pollutants
PRiF	Pesticide Residues in Food
RfD	reference dose
SACN	Scientific Advisory Committee on Nutrition
TDI	tolerable daily intake
UNEP	United Nations Environment Program

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Search strategy  
General POPs exposure search

Databases interrogated:

- EFSA
- COT
- FSA
- JECFA

Scientific publication literature search

Specific search terms:

Endosulfan/Pentachlorobenzene/Chlordecone and Toxicity

Search dates (from/to) – to present

Exclusion criteria:

- studies performed in plants and freshwater organisms
- studies involving occupational exposure
- freshwater and wastewater samples
- agricultural soil samples

Endosulfan/Pentachlorobenzene/Chlordecone and Neurotoxicity

Search dates (from/to) – to present

Exclusion criteria:

- studies performed in plants and freshwater organisms
- studies involving occupational exposure
- freshwater and wastewater samples
- agricultural soil samples

Endosulfan/Pentachlorobenzene/Chlordecone and Endocrine Disruptors

Search dates (from/to) – to present

Exclusion criteria:

- studies performed in plants and freshwater organisms
- studies involving occupational exposure
- freshwater and wastewater samples
- agricultural soil samples

Endosulfan/Pentachlorobenzene/Chlordecone AND Genotoxicity

Search dates (from/to) – to present

Exclusion criteria:

- studies performed in plants and freshwater organisms
- studies involving occupational exposure
- freshwater and wastewater samples
- agricultural soil samples

Endosulfan/Pentachlorobenzene/Chlordecone AND levels in Food

Search dates (from/to) – to present

Exclusion criteria:

- mixtures of pesticides
- contaminated land

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Endosulfan/Pentachlorobenzene/Chlordecone AND breastmilk

Search dates (from/to) – to present

Exclusion criteria:

- studies from countries other than the UK and Europe

The above mentioned search terms were also used in Google. It identified latest government advice and opinions.