ENDOSULFAN

SUMMARY

Endosulfan is an insecticide still in widespread use in many countries, on crops like cotton, soy, coffee, tea and vegetables, but also banned in 55 countries because of high toxicity to humans and nearly all other organisms, and its persistence in the environment.

Overall risk

The Intergovernmental Forum on Chemical Safety identified endosulfan as an acutely toxic pesticide that poses significant health problems for developing countries and economies in transition (IFCS 2003). However this statement of concern is no longer limited to developing countries, nor just to acute effects, nor just to humans.

European Union (GFEA-U 2007) risk statements include:

- very toxic, dangerous for the environment;
- harmful in contact with skin;
- very toxic by inhalation;
- very toxic if swallowed; and
- very toxic to aquatic organisms, may cause long term effects in the aquatic environment

The United States Environmental Protection Agency (US EPA) concluded in 2002 that endosulfan exposure can result in both acute and chronic risks in terrestrial and aquatic environments. Labels on products are required to carry the statement: “Do not allow spray to drift from the application site and contact people, structures people occupy at any time and the associated property, parks and recreation areas, nontarget crops, aquatic and wetland areas, woodlands, pastures, rangelands or animals.”

In 2007 the US EPA stated that: “occupational assessment for endosulfan indicates short- and intermediate-term risks for mixers, loaders, and applicators for the majority of uses, even with maximum Personal Protective Equipment (PPE) and engineering controls” (US EPA 2007a).

It further stated that “based upon the detection of endosulfan in areas distant from use sites, such as the Arctic, and its potential to persist and bioaccumulate, the Agency has concerns for dietary exposure of indigenous populations to endosulfan” (US EPA 2007a).

It concluded that “whilst endosulfan is not expected to biomagnify appreciably in aquatic food webs, the compound does bioconcentrate in aquatic organisms to a significant extent. Also there is direct evidence (measured residues) that endosulfan bioaccumulates in terrestrial systems and indirect evidence (modelling) that endosulfan has a significant potential to biomagnify in certain terrestrial food webs” (US EPA 2007a).

The US EPA also concluded that “desorbed residues of endosulfan volatilise and continue to recycle in the global system through a process of migration and redeposition as well as air-water exchange in the northern hemisphere” (US EPA 2007c). “Monitoring data and incident reports confirm that endosulfan is moving through aquatic and terrestrial food chains and that its use has resulted in adverse effects on the environment adjacent to and distant from its registered use sites” (US EPA 2007c).

Human Exposure

Exposure to endosulfan is high. Apart from occupational exposure which has resulted in many poisonings (see below), residues in food and drinking water are widespread globally at sufficiently high levels to constitute a threat to human health, and to result in consistent findings of human body burdens. Endosulfan contaminates breastmilk, adipose tissue, placental tissue and umbilical cord blood, meaning that the unborn child is exposed, and then re-exposed on birth through breast milk—both exposures taking place at critical periods of development where oestrogenic substances, such as endosulfan, can have a profound life-long impact.

Poisonings

There are many cases of reported poisonings—unintentional as well as intentional—resulting in death or severe disability. These have occurred principally in Asia, Africa and Latin America. Effects in survivors include congenital deformities, delayed male sexual maturity, female hormonal disorders, congenital mental retardation, cerebral palsy, psychiatric disturbances, epilepsy, cancers, skin, eye, ear, nose and throat problems, impaired memory, and chronic malaise.

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Acute toxicity

The primary acute effect is on the nervous system, causing hyperexcitation and convulsions, and nervous system mediated effects on respiration and heart. Death results from low levels of exposure.

Long-term toxicity

Endosulfan is an endocrine disruptor. It is oestrogenic and antiandrogenic in human cells, and causes breast cancer cells to grow. It also interferes with male hormones, causing chronic depression of testosterone.

It is toxic to and suppresses the immune system, as well as promoting allergic responses.

It is linked to long-term neurological effects such as epilepsy, and may cause Parkinson's disease.

Birth defects have been seen in laboratory studies and in human populations exposed to endosulfan.

Many studies show endosulfan to be mutagenic and genotoxic, and there is evidence of cancer in both laboratory animals and exposed human populations.

Environmental effects

Endosulfan is extremely toxic to fish and has caused massive fish kills. It is also highly toxic to all other aquatic organisms and demonstrates a range of chronic effects, including genotoxicity, reproductive and developmental effects. Toxicity is increased by increased temperatures: more problems can be expected with global warming.

It is also highly toxic to birds, bees, earthworms, beneficial insects and microorganisms.

Environmental contamination is widespread and has been found in soil, ground and surface waters, marine sediments, air, rainfall, snow and ice pack, grasses and tree bark all over the world—from areas in which it is still in use to high remote mountain lakes and the Arctic and Antarctic regions. Levels of contamination in aquatic systems are frequently high enough to be toxic to aquatic organisms.

Endosulfan is persistent in the environment and biomagnifies in terrestrial food chains.

Alternatives

There are many effective alternatives to endosulfan—as evidenced by its having been banned in so many countries. For example, there is a thriving organic cotton industry particularly in Africa, replacing one of the main uses of endosulfan worldwide.

Chemical Profile

Common name

Endosulfan

Common trade name

Thiodan

Other related chemicals

Technical grade endosulfan is a mixture of two isomers, alpha endosulfan (64-67%) and beta endosulfan (29-32%) (GFEA-U 2007).

Chemical names and form

6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide

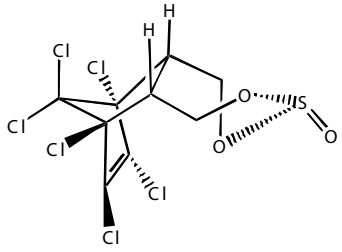
6,9-methano-2,4,3-benzodioxathiepin-6,7,8,9,10,10-hexachloro-1,5,5^{o}6,9,9-hexahydro-3-oxide

It is a cream-to-brown coloured solid that may appear crystalline or in flakes, with a distinct smell like turpentine (ATSDR 2000).

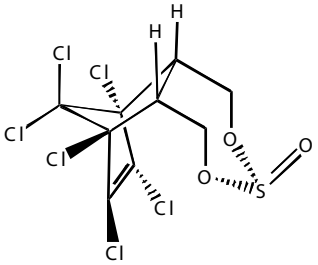
Molecular formula and structure

$C_9H_6Cl_6O_3S$

alpha endosulfan (endosulfan I):



beta endosulfan (endosulfan II):



Chemical group

Organochlorine, cyclodiene subgroup

CAS numbers

Technical endosulfan	115-29-7
Alpha endosulfan	959-98-8
Beta endosulfan	3321-65-9
Endosulfan sulphate	1031-07-8

Trade names

Trade names include: Agrisulfán, Afidan, Aikido, Akodan, Alodan, Axis, Benzoepin, Beosit, BIO 5462, Bromyx, Caiiman, Chlorbicyclen, Chlorthiepin, Crisulfan, Cyclodan, Cytophos, Devisulfan, Endel, Endocel, Endocide, Endocoral, Endocoton, Endofan, Endoflo, Endomight Super, Endopol, Endosan, Endosol, Endosulphan, Endotaf, Endoxilan, Enrofán, Ensure, ENT 23979, Flavylan 350E, FMC 5462, Galgofon, Galgptal, Global E, Goldenleaf Tobacco Spray, Hexasulfan, Hildan, HOE 2671, Insectophene, Isolan, Kop-thiodan, Lucasulfan, Malix, Misulfan, NIA 5462, Niagara 5462, Novasulfan, Palmarol, Parrysulfan, Phaser, Rasayansulfan, Red Sun, Rocky, SD-4314, Sharsulfan, Sialan, Sonii, Sulfan, Techn'ufan, Thifor, Thimul, Thiodan, Thiofanex, Thiofor, Thioflo, Thiomet, Thiomul, Thionate, Thionex, Thiosulfan, Thiosulfax, Thiokil, Thiotox, Tionel, Tionex, Tiovel, Tridane, Termizol pó, Veldosulfan, Vulcán, Zebra Ciagro.[1]

It is also found in mixtures with other insecticides, such as with methomyl in Methofan (MAI 2008), with cypermethrin in Callisulfan and chlorothalonil in Mistral (Glin et al 2006); with deltamethrin in Decisdán; and with dimethoate, isoxathion, malathion, monocrotophos, pirimicarb, triazophos, fenoprop, parathion, petroleum oils, and oxine-copper (El Hindi et al 2006; GFEA-U 2007).

It is available as emulsifiable concentrate, wettable powder, ultra-low volume liquid, and smoke tablets (GFEA-U 2007).

Inerts and contaminants

Inerts may include unidentified alcohol solvent emulsifiers, petroleum distillate emulsifiers, suspension agents, talc, and wetting agents (ATSDR 2000). Since these components are unidentified, their contribution to the hazardous effects of formulated endosulfan products is unknown.

The Environmental Risk Management Authority of New Zealand (ERMANZ 2007b) identified common impurities in technical grade endosulfan as endosulfan alcohol, endosulfan ether, hexchlorocyclopentadiene, and residual solvent.

Endosulfan is also contaminated with pentachlorobenzene (PeCB). This chemical is a Persistent Organic Pollutant (POP) (still undergoing evaluation). It is persistent, highly acutely toxic to aquatic organisms and acutely toxic to humans, and is fetotoxic (POPRC 2007).

Epichlorohydrin is reported to have been used as a stabiliser in technical grade endosulfan and it is not known if it is still used. Epichlorohydrin is mutagenic and carcinogenic in animals, and possibly carcinogenic in humans. It causes sterility in male rats, and damages the central nervous system, respiratory tract, liver, blood, eyes, and skin (ATSDR 2000).

At least one study has found a formulated product (Techn'ufan) to be more toxic than the technical grade endosulfan, causing damage to proteins specific to pulmonary cells in humans (Skandrani et al 2006).

Metabolites

The principle metabolite is endosulfan sulphate. Other metabolites include endosulfan diol, endosulfan ether, endosulfan hydroxy carboxylic acid, endosulfan hydroxyether, and endosulfan lactone (GFEA-U 007).

Endosulfan sulphate is usually included with the alpha and beta isomers of endosulfan as 'total endosulfan', or 'endosulfan (sum)' in measurement of residues. The sulphate is regarded as being equally toxic and of increased persistence in comparison with the parent isomers (US EPA 2007a).

Mode of Action in Insects

Endosulfan is a non-systemic insecticide and acaricide with contact and stomach action (Kidd & James 1991).

Uses

Endosulfan is used to control a wide range of sucking and chewing insects including aphids, thrips, beetles, foliar feeding caterpillars, mites, borers, cutworms, bollworms, bugs, whiteflies, leafhoppers, snails in rice paddies, earthworms in turf, and tsetse flies.

Major crops to which it is applied include soy, cotton, rice, and tea. Other crops include vegetables, fruit, nuts, berries, grapes, cereals, pulses, corn, oilseeds, potatoes, coffee, mushrooms, olives, hops, sorghum, tobacco, and cacao. It is used on ornamentals and forest trees, and has been used in the past as an industrial and domestic wood preservative (ERMANZ 2007b; GFEA-U 2007; Kidd & James 1991).

Endosulfan is reported to be one of the most commonly used pesticides in India in recent years, particularly on rice and cotton against thrips, stem borer, whorl maggot, case worm, boll worm and bud worm (Jayashree & Vasudevan 2007b).

It is used to control ectoparasites on farm animals and pets in Ghana (Darko & Acquaah 2008).

It is also used on sand-based sports fields in New Zealand to kill earthworms and prevent formation of worm casts (Tasman District Council 2008) and there are anecdotal reports that it is also used on the grass strips between aircraft runways again to kill earthworms, which might encourage the presence of birds.

In May 2007 Codex Alimentarius cancelled maximum residue limits (MRLs) for endosulfan in a number of crops including apple, broad bean, cabbage, carrot, cauliflower, common bean, cotton seed oil, garden peas, grapes, lettuce, maize, onion, orange, peach, pineapple, plums,

rape seed, rice, spinach, sugar beet, sunflower seed, and wheat. These uses are no longer supported.

However they adopted MRLs for avocado, broccoli, cacao beans, celery, cherries, coffee beans, cottonseed, cucumber, custard apple, eggplant, hazelnuts, litchi, macadamia nuts, mango, melons, papaya, persimmon, potato, soybean, squash, sweet potato, and tomato.

Due to pressure from India and China MRLs for tea will continue for 4 years (Codex 2007).

Manufacturers

Endosulfan was developed in the early 1950s and registered by Hoechst in 1954 in USA. Its ownership then transferred, as companies merged and split, to AgroEvo, then Aventis CropScience, and finally Bayer CropScience.

Global production of endosulfan was estimated to be 10,000 tonnes annually in 1984. Current production is judged to be significantly higher. Li & Macdonald (2005) published an estimate in 2005 of 338,000 tonnes *cumulative* global usage on crops, and noted a general trend of increasing total global use of endosulfan, although it is possible that the dip they observed in usage figures around 1999 has continued downwards.

India is regarded as being the world's largest producer and user (Li & Macdonald 2005), with more than 60 endosulfan manufacturers and formulators, mostly the latter (WebIndia 2007). Production began in 1996 (GEF IO 2002), and by 2004 India had become the leading producer of endosulfan, with three companies—Coromandel Fertilisers Ltd, Excel Crop Care, and Hindustan Insecticides Ltd (Venkatraman 2004; CFL 2008). Excel is the largest of the three, with a reported capacity of 6,000 tonnes per annum (Yadav & Jevan undated). Hindustan Insecticides produces 1,600 tonnes per annum at its facility in Kerala (HIL 2008). Production figures for Coromandel Fertilisers's Mumbai plant are not available. WebIndia (2007) reports that 70% of India's production is exported.

Germany is the worlds' second largest producer of endosulfan, with Bayer CropScience producing approximately 4,000 tonnes per annum at its Frankfurt plant. Most of this is exported to Southeast Asia, Latin America, and the Caribbean (GFEA-U 2007).

Li et al (2007) stated that China was producing about 2,400 tonnes per year although gave no date for this figure. Endosulfan is manufactured in China by a number of companies: in 2005 there were 3 manufacturers in Jiangsu province, and 40 formulators mostly located in Shangdong and Jiangsu provinces (Jia et al 2008). In 2007, there were reported to be four manufacturers in Jiangsu province: Jiangsu Kuaida Agrochemical Co, Jiangsu Xuzhou Shengnong Chemicals Co, Huangma Agrochemical Co, and Zhangjiagang Tianheng Chemical Co (Sun Jing 2007).

It is also manufactured in Israel (Makhteshim-Agan Industries), and is reported to be manufactured in South Korea.[2]

Regulatory status

Endosulfan is banned or restricted in many countries because of human health and environmental impacts.

Countries that have banned endosulfan include Bahrain, Belize, Cambodia, Colombia, Cote d'Ivoire, Jordan, Kuwait, Malaysia, Norway, Oman, Qatar, Saudi Arabia, Singapore, St Lucia, Sri Lanka, Syria, and United Arab Emirates.[3] In February 2008, Benin announced that endosulfan would be banned once existing stocks are used (Anon 2008). Nine West African countries have recently banned the use of endosulfan in cotton, believed to be its only use in these countries—Senegal, Mauritania, Mali, Guinea Bissau, Burkina Faso, Tchad, Cap-Vert, Gambia, and Niger (Correra 2007). There is also an unconfirmed report that it has been banned in Nigeria (Shaibu 2008).

Endosulfan is effectively banned in all the European Union countries, as it was not included in Annex 1 of Council Directive 91/414 (EU 2005). This brings the total of countries known or believed to have banned endosulfan to 55.

It is also banned in the state of Kerala, India, as a result of severe adverse effects arising from aerial spraying of endosulfan on cashew plantations, and in 2006 the government of Kerala State announced relief and remediation for the affected villages of Kasargod community whose health has been badly damaged by the spraying (Chelaton & Sridhar 2006).

Countries that have restricted endosulfan include Australia, Bangladesh, Canada, Honduras, Iceland, Indonesia, Iran, Japan, Korea, Madagascar, Panama, Philippines,[4] Russia, Thailand, USA, and UK.[5]

Brazil, Canada, USA, Uruguay, Venezuela, and New Zealand are reassessing endosulfan.

International regulatory action

In July 2007, the Council of the European Union made the decision to propose endosulfan for listing in the Stockholm Convention on Persistent Organic Pollutants for global elimination (EU 2007).

In March 2007, the Chemical Review Committee of the Rotterdam Convention on the Prior Informed Consent Procedure agreed to forward to the Conference of the Parties of the Convention the recommendation for inclusion of endosulfan in Annex III. Annex III is the list of chemicals that have been banned or severely restricted for health or environmental reasons by Parties, and the exporting of which requires prior informed consent from the proposed recipient country. This recommendation was made on the basis of the notification of a ban by the Netherlands and severe restriction by Thailand (UNEP/FAO 2006a). The European Union, Cote d'Ivoire, Jordan and Norway have also notified their bans to the Secretariat. The PIC

procedure will require that endosulfan is exported only to those countries that specifically allow its importation.

Endosulfan is listed in the European Union's water policy's Annex X as a priority substance for control of pollution in the aquatic environment (EU 2001).

Endosulfan has been included in the List of Chemicals for Priority Action by the OSPAR Commission for the Protection of the Marine Environment in the North-East Atlantic because of pollution in the marine environment (OSPAR 2006); and is on the list of priority substances agreed by the Third North Sea Conference (UK Marine Sacs undated).

In the UNEP-GEF Regional-based Assessments of Persistent Toxic Substances (PTS), it is rated as:

- Indian Ocean region—regional concern (GEF IO 2002);
- North American region—regionally specific PTS (GEF NA 2002);
- Mediterranean region—local concern (GEF M 2002);
- Sub Saharan Africa—PTS of highest concern after DDT (GEF SSA 2002);
- East and West South American—emerging concern (GEF SA 2002);
- European region—proposed possible priority hazardous substance (GEF E 2002);
- South East Asia and South Pacific region—regional concern, with long-term effect on the structure of the aquatic ecosystem (GEF SEA SP 2002); and
- Central America and Caribbean—one of the most important PTS of emerging concern (GEF CAC 2002).

Toxicological Assessment

Absorption and distribution

In animals absorption through the gastrointestinal tract is very rapid and efficient, with >90% absorbed in rats. Absorption through the skin has been as high as 50% in rats (GFEA-U 2007).

Endosulfan is readily metabolised in animals by microsomal enzymes, initially to endosulfan sulphate and endosulfan diol; and excreted in urine and faeces. It has been found distributed to adipose, liver, kidney, heart, spleen, testes, epididymis, prostate, seminal vesicle, milk and muscle. There is a greater accumulation in adipose tissue of females than males, possibly because of more rapid excretion by males. One study in rats concluded that it is rapidly eliminated from the body after ingestion ceased, with an estimated half-life of approximately 7 days (ATSDR 2000).

Mode of action in mammals

Endosulfan has an affinity with the GABA (gamma-aminobutyric acid) receptors in the brain and acts as a non-competitive GABA antagonist. Binding of GABA to its receptors induces the uptake of chloride ions by neurons and blockage of this uptake by endosulfan results in a state of uncontrolled excitation (UNEP/FAO 2007).

Acute toxicity

Tests are generally carried out using technical grade endosulfan, which consists of both alpha and beta endosulfan. Alpha endosulfan is about 3 times more toxic than beta (ATSDR 2000).

US EPA (2002) toxicity categories:

- oral – category I: highly toxic
- inhalation – category II: moderately toxic
- dermal – category III : slightly toxic

World Health Organisation Recommended Classification by Acute Hazard (WHO 2005):

- Class II moderately hazardous.

UNEP/FAO (2007) describes endosulfan as being highly toxic through oral or dermal exposure.

Lethal doses

Lethal dose, LD_{50}, is the dose that kills 50 % of test animals. LD_{50}s for endosulfan are:

- Oral LD_{50} rat
  = 10- 23 mg/kg (female); 48-160 mg/kg (male)
- Dermal LD_{50} rat
  = 500 mg/kg (female); >4000 mg/kg (male)
- Inhalation LC_{50} rat
  = 0.0126 mg/l (female); 0.0345 mg/l (male). (GFEA-U 2007)

Acute effects

The primary effect of acute exposure is on the nervous system.

Inhalation: ataxia, hyperexcitability, trembling, convulsions, reduced reflexes of the cornea, pupil and skin; irregular respiration, and lung lesions (ATSDR 2000).

Oral: hyperactivity and hyperexcitation, seizures, tremors, convulsions, clonic spasms, brain oedema, salivation, dilated pupils, poor muscle tone, head swaying, vomiting, diarrhoea, rapid respiration, decreased respiration, noisy breathing, shortness of breath, lung congestion, emphysema, cyanosis, respiratory paralysis, haemorrhage of heart muscle, lung and kidney; death (ATSDR 2000).

Dermal: shortness of breath, increased respiratory rate, rapid heart rate, decreased heart rate, nausea, vomiting, abdominal pain. Endosulfan has also caused death of livestock (calves) and laboratory animals through a single dermal exposure (ATSDR 2000).

Skin and eye irritation

Skin: mild irritation in rats, including erythema, slight oedema and dry rough scaling skin (ATSDR 2000).

Eyes: category I irritant, causing residual opacity (US EPA 2002).

No and Lowest Observed Adverse Effects Levels
The No Observed Adverse Effects Level (NOAEL) is the lowest dose of the chemical given to a test animal at which no effects are observed, and the Lowest Observed Adverse Effects Level (LOAEL) is the lowest dose of the chemical given to a test animal at which an effect is observed.

- NOAEL (acute oral, rat) = 1.5 mg/kg/day (US EPA 2002)
- NOEL (acute oral, rabbit) = 0.7 mg/kg/day (CAL EPA 2007)
- LOAEL (acute oral, rat) = 3 mg/kg/day, causing convulsions in female rats within 8 hours of dosing (US EPA 2002). However ATSDR (2000) reported the lowest LOAEL as 1.8mg/kg/day causing convulsions in pregnant rabbits after 10 days of force-feeding endosulfan.

Sub-chronic toxicity / intermediate

The sub-chronic NOAELs and LOAELs are:

- NOAEL = 3.85 mg/kg/day (male rat), 2.3 mg/kg/day (mice)
- LOAEL = 23.41 mg/kg/day (male rat), 7.4 mg/kg/day (mice) (ATSDR 2000)
- LOAEL (short-term dermal) = 3.74 mg/kg/day (rat) (US EPA 2007b)
- NOAEL (short-term inhalation) = 0.2 mg/kg/day (rat) (US EPA 2002, 2007a)

Systemic effects
The primary systemic targets are the liver and kidney, but it also causes haematological and respiratory effects as a result of generalised effects on the central nervous system.

Observed effects on rats include:

- inflammation of lungs;
- congestion and degeneration of kidney tubules renal necrosis, renal haemorrhage;
- congestion and necrosis of the liver;
- blood in small intestines, diarrhoea;
- decreased haemoglobin and red blood cell count in protein deficient rats;
- damage to the membrane of red blood cells, increasing permeability and impairing enzyme activity, even at very low doses (1 *u*g/kg) that are 500-fold lower than the generally permissible level for residues in food of 500 *u*g/kg;
- calcification of heart and coronary and mesenteric arteries, aneurisms, cardiotoxicity through oedema and swelling of myocardial cells, heart and circulatory failure;
- reduced body weight gain, reduced appetite; and
- hyperglycaemia, more marked in older animals (Daniel et al 1986, ATSDR 2000; Choudhary et al 2003).

Endosulfan is toxic to both the adrenal gland and the pancreas, causing degranulation of the beta cells of the islets of Langerhans in the later (ATSDR 2000). The resulting effects on blood glucose levels are complex:

- On the one hand it is toxic to adrenocortical cells in fish (at low doses that do not decrease cell viability) and impairs their production of cortisol (Bisson & Hontela 2002; Dorval et al 2003). Cortisol is antagonistic to insulin and promotes the breakdown of glycogen, which then increases blood sugar levels—so in this instance endosulfan acts to **reduce** blood sugar levels by reducing cortisol.
- On the other hand, in the pancreas of rats it is toxic to the B cells of the islets of Langerhans, which produce the insulin necessary to reduce blood sugar levels, so in this case it acts to **raise** blood sugar levels (Kalender et al 2004).

Endosulfan causes oxidative stress (Omurtag et al 2008), which is implicated in its neurotoxic effects (Jia & Mizra 2007a,c), damage to the adrenal gland (Dorval & Hontela 2003; Dorval et al 2003), and in cancer (Antherieu et al 2007). The brain is particularly sensitive to oxidative damage from sublethal levels of endosulfan, at least in fish (Ballesteros et al 2008).

Chronic toxicity

The chronic NOAEL and LOAEL are:

- NOAEL = 0.57 mg/kg/day (female dog), 0.67 mg/kg/day (male dog)
- LOAEL= 1.75 mg/kg (dog)

Immune system
The immune system is more sensitive, reacts more rapidly, and at lower doses, to the effects of pesticides than other organ systems, so effects on this system can indicate subclinical toxic states (Pistl et al 2003).

A number of studies show that endosulfan is toxic to, and suppresses, the immune system, as well as promoting allergic responses.

Endosulfan induces immunosuppressive effects—decrease in humoral antibody and cell-mediated immune response—at low dose levels that do not induce any other sign of toxicity; and decreases macrophage function (ATSDR 2000). The ATSDR (2000) concluded humans may be at risk of adverse immune effects following exposure to endosulfan. Effects include decreased serum IgG levels, decreased antibody titer to tetanus toxin, inhibition of leukocyte and macrophage migration, and increased albumin-to-globulin ratio (ATSDR 2000; Abadin et al 2006).

It was also immunosuppressive and immunotoxic in sheep blood cells, causing significant suppression of phagocytes, decreased activation of lymphocytes, and decreased migration of leukocytes (Pistl et al 2003).

In broiler chicks, endosulfan reduced total leucocytes, T-lymphocytes, macrophages, and caused atrophy and haemorrhage of the thymus gland (Garg et al 2004).

Endosulfan is highly immunotoxic to fish, causing suppression of phagocytic function of the head kidney immune cells of Australian freshwater fish (Harford et al 2005).

Exposure to endosulfan *in utero* and through postnatal lactation resulted in immunosuppressive effects on adult rats, with female rats being more susceptible than males (Lafuente et al 2006).

Endosulfan promotes allergic disease in humans by enhancing mast cell degranulation: it caused rapid, dose-related release of β–hexosaminidase (a marker for the granules that contain preformed allergic mediators) from human mast cells, and enhanced IgE-mediated release (Narita et al 2007).

Endosulfan also induces the death of human Natural Killer T-cells, which are part of the immune system involved in tumour suppression (Kannan et al 2000), hence endosulfan assists the development of tumours.

Endocrine disruption

Endosulfan is an endocrine disruptor in mammalian species, and in fish, birds and amphibians, affecting both male and female reproductive hormones.

In male rats endosulfan caused a dose-related decrease in testosterone, luteinizing hormone and follicular stimulating hormone, with depressed activity of steroidogenic enzymes and testicular cytochrome P450-dependent monoxygenases. The testosterone remained chronically depressed, but the other effects were reversible. ATSDR (2000) concluded that endosulfan may potentially cause reproductive toxicity in humans.

Studies of the effects on female hormone levels in animals are inconsistent. However studies on human cells indicate that endosulfan is oestrogenic, interfering with the steady state levels of oestrogen receptors (Grunfeld & Bonefeld-Jorgensen 2004); and causing proliferation of MCF-7 human oestrogen-sensitive breast cancer cells (Soto et al 1994, 1995; Bonefeld-Jorgensen et al 2005), and oestrogen-sensitive ovarian cells (Wong & Matsumara 2006). The simultaneous exposure of breast cancer cells to endosulfan and growth factors increased the oestrogenic effect of endosulfan on cell growth (Cossette et al 2002). It activates the oestrogen receptor (ER) alpha but weakly antagonises ER beta. This increases its harmful action: because ER beta can oppose the cell proliferation effects of ER alpha, antagonising ER beta increases the risk of cell proliferation (Lemaire et al 2006).

Other studies have demonstrated the oestrogen-mimicking effect of endosulfan on enzymes in pituitary tumour cells (Bulayeva & Watson 2004) and in breast cancer cells (Li et al 2006a), which subsequently leads to cell proliferation, transformation, differentiation and migration. In Bulayeva & Watson's study, the oestrogenic effect of endosulfan showed a bimodal response: it occurred at very low subpicomolar levels and at higher levels, but not medium levels, a similar response pattern to that of the natural hormone oestradiol.

As well as mimicking oestrogen, endosulfan is also anti-androgenic (Andersen et al 2002; Kojima et al 2004; Chatterjee et al 2008). It also induces the activation (Hunter et al 1999) and proliferation of progesterone receptors—another oestrogen-mimicking effect—in human breast cancer cells (Soto et al 1995), and it decreases the activity of progesterone (Jin et al 1997; Chatterjee et al 2008).

Exposure to endosulfan at very low concentrations may cause breast cancer by interfering with a number of hormonal mechanisms:

- It has recently been found to activate aromatase in cancer cells in the human placenta at low concentrations that do not cause cytotoxicity (Laville et al 2006); aromatase is the enzyme that catalyses conversion of androgens to oestrogen.
- It significantly increases the ratio of 16-hydroxyestrone (a tumour promoting oestrogen) to 2-hydroxyestrone (non-genotoxic), increasing breast cancer cell proliferation, development, and promotion (Bradlow et al 1995).
- It potentiates 17*beta*-estradiol (Andersen et al 2002), the primary natural oestrogen, elevated levels of which are strongly linked to breast cancer (Toniolo et al 1995; Berrino et al 1996; Dorgan et al 1996).
- It causes changes to intracellular oestrogenic signalling that increase the risk of breast cancer at very low concentrations (e.g. 10^{-10} M)—by mimicking the effects of oestrogen and raising cellular calcium levels, which then cause rapid secretion of prolactin which in turn causes cell proliferation (Rousseau et al 2002; Wozniak et al 2005; Watson et al 2007).

Endosulfan interferes with mammary gland development—increasing the number of alveolar buds—by increasing telomerase reverse transcriptase mRNA transcriptional activity (Je et al 2005).

Endosulfan's ability to act as a xeno-oestrogen may also cause it to contribute to cervical cancer and endometriosis, which are regarded as being oestrogen dependent disorders (Lemaire et al 2006; Foster & Agarwal 2002).

Nervous system

Endosuflan targets the prefrontal cortex of the brain, which is involved in cognitive tasks, selective attention, short-term working memory, response inhibition, behavioural flexibility, sexual and maternal behaviour, and depression (Cabaleiro et al 2008).

Endosulfan changes the brain levels of the neurotransmitters dopamine, noradrenalin and serotonin (ATSDR 2000). In particular, endosulfan blocks the receptors for the GABA neurotransmitter in nerve cells (Vale et al 2003). GABA neurotransmission is important in gestational brain development (Roberts et al 2007). It also has age-related effects on other amino acids in the prefrontal cortex of the brain (Cabaleiro et al 2008).

There is emerging evidence that exposure to endosulfan may increase the risk of Parkinson's disease. Mice exposed to endosulfan from postnatal days 5 to 19 exhibited only insignificant changes in dopamine, acetylcholinesterase and alpha-synuclein levels; however when re-exposed as adults they showed significantly depleted dopamine, increased levels of alpha-synuclein and increased acetylcholinesterase activity in the brain (Jia & Misra 2007a). Endosulfan, at low concentrations

(10nmol/l-10*u*mol/l) also inhibits proteasome activity—which degrades proteins like alpha-synuclein (Wang et al 2006a). The loss of dopamine and the accumulation of alpha-synuclein are both associated with Parkinson's disease.

Low doses of endosulfan reduced the threshold for seizures produced by electrical stimulation in rats (ATSDR 2000).

Endosulfan can cause behavioural effects such as aggression and increased time to learn tasks, even after exposure has ceased; and impaired learning and memory processes, extreme sensitivity to noise and light, and muscle spasms (ATSDR 2000).

Reproductive & developmental effects

- LOEL (repro) = 6.2 mg/kg/day (rat)
- NOEL (devel) = 2.0 mg/kg/day (rat)
- LOEL (devel) = 6.0 mg/kg/day (rat)

(ATSDR 2000)

Endosulfan has caused a number of adverse effects on male reproductive parameters in rats, reducing fertility: degeneration of seminiferous tubule epithelium, reduced sperm count, altered spermatogenesis, increased abnormal sperm, testicular necrosis, and aspermatogenesis (Dalsenter et al 1999; ATSDR 2000; Sinha et al 2001). Effects were reported to be greater if exposure occurred during the developmental phase (Saiyed et al 2003). Adverse effects on male offspring have occurred even at dose levels that were not toxic to the mother (Sinha et al 2001).

ATSDR (2000) concluded that, for humans, exposure during the period of testicular maturation may result in disturbed spermatogenesis at sexual maturity (ATSDR 2000).

Endosulfan has also been shown to reduce implantation in female mice, and to increase oestrus (Hiremath & Kaliwal 2002).

Exposure *in utero* to endosulfan has caused embryotoxic effects in animal studies including increased resorptions and skeletal variations, decreased birth weight and length, and increased aggressive behaviour in newborn rats, but the findings are regarded by the ATSDR (2000) as inconclusive. More recently Singh et al (2006) reported similar teratogenic effects, as well as accumulation of cerebrospinal fluid in the brain, underdeveloped cerebrum, incomplete ossification of skull bones, and malformations of the liver, kidneys, ribs and renal pelvis.

A study with human sperm *in vitro* showed that low concentrations of endosulfan (0.1nM) strongly inhibited the ability of sperm to fertilise ova (ATSDR 2000).

Endosulfan disrupts the retinoid signalling pathway in cells, and this is thought to explain the teratogenic effect of long-term exposure to low levels of the chemical, as has been experienced in India (congenital heart and skeletal abnormalities). Retinoids play an essential role in the proliferation, development and differentiation of cells and disruption can lead to malformation or abnormal development of the eye, brain, heart, and limbs (Lemaire et al 2005).

Genotoxicity / mutagenicity

Studies have yielded inconsistent results leading ATSDR (2000) to conclude it is not genotoxic in rats.

However, endosulfan has caused mutagenic and genotoxic effects in human lymphocytes and liver hepatoblastoma cells; in rat and mouse spermatogonial cells; in rat, mouse and hamster bone marrow; in rat foetal liver cells; in fruitfly; in fish gill, kidney and erythrocyte cells; in tadpoles; in oysters; in Chinese hamster ovarian cells; in bacterial systems (*Salmonella*, *E. coli* and *Saccharomyces*); in microalgae; and in the root tip cells of the wetland macrophyte *Bidens laevis* L (Yadav et al 1982; Sobti et al 1983; Pandey et al 1990; Lu et al 2000; ATSDR 2000; Jamil et al 2004; Lajmanovich et al 2005; Bajpayee et al 2006; Neuparth et al 2006; Pandey et al 2006; Antherieu et al 2007; Sharma et al 2007a; Wessel et al 2007; Akcha et al 2008). The effects include formation of DNA adducts, DNA strand breaks, sister chromatid exchange, micronucleus induction, chromosomal aberrations and gene mutations. Of the 27 studies reported by the ATSDR, 17 were positive for genotoxic effects. Sister chromatid exchange was increased at least 5-fold in rat embryos. ATSDR (2000) described endosulfan as an 'efficient' mutagen in *Drosophila* (fruit fly), and concluded that the data showed endosulfan to be mutagenic and clastogenic, although some of this effect may be caused by the stabiliser epichlorohydrin used in some formulations.

In a first attempt to test endosulfan's genotoxicity in plants, Perez et al (2007) found it to be genotoxic to the wetland macrophyte *Bidens laevis* L (bur marigold, beggars tick) at environmentally relevant concentrations. It interacted with the mitotic spindle at concentrations of only 5 *u*g/l, well below the NOAELs reported for chronic toxicity (0.57, 0.67 mg/kg/day). In microalgae it caused DNA strand breaks at concentrations of only 1 *u*g/l (Akcha et al 2008). Both these findings of genotoxicity occurred at doses well below concentrations found in the aquatic environment (run-off in Southern USA has contained concentrations as high as 100 *u*g/l, in India up to 66.5 *u*g/l, and in Australia up to 45 *u*g/l (Menone et al 2008)).

GFEA-U (2007) concluded that there is evidence of mutagenicity, clastogenicity and effects on cell cycle kinetics.

Cancer

Evidence of the carcinogenicity of endosulfan is regarded as being inconclusive. Some studies have found an increase in the total number of malignant tumours and pulmonary adenomas, and increases in total number of carcinomas, hepatic carcinomas, and sarcomas in female rats, and lymphosarcomas in male rats (e.g. Reuber 1981). However the poor quality of the studies precludes firm conclusions according to ATSDR (2000).

Alpha endosulfan is a tumour promoter causing a significant and dose-related increase in hepatocytes (liver cancer cells) (Fransson-Steen et al 1992; ATSDR 2000), and to rapidly inhibit gap junctional intercellular communication (GJIC) in liver cells (Dubois et al 1996; Warngard et al 1996). The tumour promoting effect is suggested to be through the inhibition of GJIC (ATSDR 2000).

Endosulfan has not been classified by the International Agency for Research on Cancer (IARC) as a carcinogen, and was described by the International Programme on Chemical Safety (IPCS) (2000) as not carcinogenic, but it is increasingly being described as a potential carcinogen in humans (Antherieu et al 2007). The authors of this recent study found that it generates reactive oxygen species causing oxidative stress, and that this results in endosulfan having mutagenic effects and causing increased DNA strand breaks. It was found to inhibit apoptosis, which "could contribute to mutant cell survival and therefore have possible carcinogenic effects". Sohn et al (2004) demonstrated that endosulfan induces oxidative stress and inhibits cellular respiration via the generation of reactive oxygen species. Oxidative stress is also described in the section on Systemic Effects.

Other effects

Endosulfan has been shown to be a nonspecific inducer of drug metabolism by inducing microsomal enzyme activity (ATSDR 2000).

Toxic interactions

Alcohol may interfere with the metabolism of endosulfan delaying its elimination from the body and increasing its toxic effect (ATSDR 2000).

There is also a suggestion that dimethoate and endosulfan act synergistically in human poisoning (ATSDR 2000).

Endosulfan in combination with methyl parathion significantly increased adverse effects on rat behaviour compared with dosage of either of the pesticides alone, even at doses that did not cause overt toxicity, or kidney or liver pathology (Castillo et al 2002).

Endosulfan and zineb in combination exhibited significantly higher toxicity to human cells than either by itself (Jia & Misra 2007b).

Endosulfan increases the potency of the drug diazepam (ATSDR 2000).

Endosulfan increases the convulsant action of picrotoxin, a poisonous alkaloid in a fruit from Southeast Asia known as ligtang, aria, bayat, Indian berry or Levant nut (ATSDR 2000).

Gender differences

Female rats are 4-5 times more sensitive to the lethal effects of endosulfan than male rats. There is a lack of data to determine if this is also true of other species (ATSDR 2000). The difference is attributed to differences in metabolism of endosulfan.

Sensitive populations

A protein deficient diet caused a 20-fold increase in sensitivity to the lethal effects of endosulfan in rats. It also enhances the anaemia-inducing capacity of endosulfan (ATSDR 2000).

Increased mortality also occurred in pregnant rats (ATSDR 2000).

The foetus and newborns are more sensitive than adults at least for neurotoxic effects (ATSDR 2000).

The ATSDR (2000) lists the following groups of people who may be particularly vulnerable to the effects of endosulfan:

- people with liver or kidney disease, pre-existing anaemia or haematologic disorders, or neurological problems especially seizure disorders such as epilepsy;
- people with compromised immune systems such as AIDS/HIV patients, infants and the elderly; and
- people with protein-deficient diets such as the malnourished poor, chronic alcoholics, dieters, and the elderly.

It is possible that diabetics may also be at increased risk from endosulfan, given its complex effects on blood glucose levels including the ability to significantly elevate them (Kalender et al 2004). Additionally endosulfan, in a mixture with hexachlorocylclohexane (HCH) and monocrotophos, was more toxic to diabetic rats and especially those that were also malnourished than to healthy rats (Benjamin et al 2006).

Human Exposure

Exposure guidelines

EU:

- ADI (acceptable daily intake) = 6 *u*g/kg bw
- ARfD (acute reference dose) = 15 *u*g/kg bw

(UNEP/FAO 2006b)

US:

- Minimum Risk Level (acute, oral) = 5 *u*g/kg/day
- Minimum Risk Level (chronic, oral) = 2 *u*g/kg/day

(ATSDR 2000)

Occupational exposure

In 2007, the US EPA concluded that "occupational assessment for endosulfan indicates short- and intermediate-term risks for mixers, loaders, and applicators for the majority of uses, even with maximum Personal Protective Equipment (PPE) and engineering controls" (US EPA 2007a).

Protective clothing requirements in the USA are a coverall over long-sleeved shirt and long pants, chemical resistant footwear plus socks, chemical resistant gloves, chemical resistant head gear when exposed overhead and a respirator (US EPA 2002).

Occupational exposure has resulted in residues of endosulfan and its metabolites in the blood of agricultural workers who sprayed endosulfan in greenhouses in Spain (Arrebola et al 2001), and in residues in the male offspring of women agricultural workers in Spain (Carreno et al 2007), as well as numerous fatalities and severe adverse health effects globally (see Symptoms and Consequences of Poisonings and Cases of Poisonings).

Non-occupational exposure

Non-occupational exposure is very common. In France endosulfan was found to be a ubiquitous air pollutant in residences in the Paris area, found in 79% of homes, and in some of them at levels higher than those found in greenhouses. At this stage (2006) endosulfan was still permitted for use in France but only on some fruit and vegetables, and its presence in homes appeared to result from drift and contaminated plant matter. It was also found, on the hands of 20% of the general population sampled in Paris (Bouvier et al 2006).

Reuse of containers

Reuse of containers for storing food, water, milk, oil, etc, or as drinking vessels, has caused a number of poisonings. For example, in Benin an 8 year old died after using a discarded Callisulfan container to scoop drinking water from a canal (Glin et al 2006).

Contaminated clothing

Contaminated work clothing can be a problem; for example in Benin 4 children died after work clothes left on the roof of a house after spraying were exposed to overnight rain that leached out the endosulfan into the vessel used for drinking water (Glin et al 2006).

Residues in food and drink[1]

Non-occupational exposure frequently occurs as a result of residues in food and drinking water. Such residues are commonplace where endosulfan is used, and are of such magnitude in some countries as to constitute a significant risk to health. Residues also contribute to the body burden of endosulfan. Campoy et al (2001) found a positive correlation between intake of contaminated vegetables and the presence of endosulfan-lactone in breast milk in Spain. Deaths have been reported from consuming contaminated fish after East African fishermen used endosulfan for catching it (GFEA-U 2007); and two people are reported to have suffered neurological symptoms are consuming food contaminated with endosulfan in Turkey (Oktay et al 2003).

Endosulfan contamination of vegetables and fruit is widespread. It was one of the most commonly detected residues in the 5000 most widely consumed foods in the USA, and in fruit and vegetables in Europe (Campoy et al 2001). Between 2001 and 2006 it was found in oil, strawberries, peppers, celery and cucumber in Barcelona, Spain (Fontcuberta et al 2008); in red pepper and eggplant from Italy; and in vegetables and grapes from Cyprus (GEF M 2002). An analysis of organic waste material in Germany found high concentrations in lettuce and smaller amounts in tropical fruit peels and flowers (Taube et al 2002).

In New Zealand 32% of tomatoes sampled contained endosulfan with levels up to 972 *u*g/kg (NZFSA 2007). It has also been found in capsicum, courgette, cucumber, pears, vegetable oil, salad dressing, peanuts and peanut butter. Eating only one tomato per day, without the other foods, results in a daily intake of approximately 81 *u*g of total endosulfan, or 1.18 *u*g/kg of body weight for the average woman (68.7 kg), for one out of three women. Endosulfan intake is likely to be higher than this given the residues in other foods. Subclinical adverse effects could result from this level of intake considering that dose levels of only 1 *u*g/kg have caused damage to red blood cells, increasing permeability and impairing enzyme activity in rats (Daniel et al 1986), and 0.5 *u*g/l has caused DNA damage in fish (Sharma et al 2007a).

In India, all samples of cauliflower, brinjal and okra taken at Ranchi, Jharkhand were found to contain endosulfan at levels as high as 2,470 *u*g/kg (Shahi et al 2005); and almost all samples of the fruits ber, grapes and guava (Kumari et al 2006). It is also found in rice (Jayashree & Vasudevan 2007b) and mangoes (Singh et al 2008a) in India. It has been found in sesame seeds, groundnuts, chilli powder in India; and in canned pineapple, chillies and onion in Sri Lanka (GEF IO 2002). 100% of 28 samples of a complete daily vegetarian diet, taken in Hisar City, were contaminated with endosulfan, with residues up to 354 *u*g/kg (Kumari & Kathpal 2008).

It has been found in Ghana, in 36% of lettuces at up to 1,300 *u*g/kg, which is nearly 3 times the MRL (Amoah et al 2006). It was found in pekmez, the traditional grape molasses of Turkey (Erdogrul 2007b). It has been found in vegetables in El Salvador and Colombia (GEF CAC 2002), Argentina, and in tomatoes in Brazil (Araujo et al 1999).

Endosulfan has even been found in leeks that were not treated with the pesticide, efficiently removing it from the soil (Gonzalez et al 2003). In fact the authors suggested that leeks may be grown as a means of decontaminating the soil.

Endosulfan has been reported to contaminate animal feed (Deka et al 2004), and to be excreted in goats milk when goats ingest it even up to 20 days after ingestion ceases (Nag et al 2007). It has been found in 27% of cows' milk samples in Bundelkhand (Nag & Raikwar 2008) and Haryana in India (Sharma et al 2007b), Brazil (Ciscato et al 2002), Colombia (GEF CAC 2002), and Argentina (Maitre et al 1994); in butter with 11% of samples above

1 For residues throughout this document, unless otherwise specified, the values given are for total endosulfan i.e. alpha + beta + the sulphate. Otherwise, AE = alpha endosulfan; BE = beta endosulfan, ES = endosulfan sulphate

the MRL in Haryana (Kumari et al 2005); and in butter in Turkey (Nizamlioglu et al 2005). It has recently been found in fresh milk (0.12 *u*g/kg), yoghurt (0.34 *u*g/kg), and cheese (9.06 *u*g/kg) in Ghana (Darko & Acquaah 2008).

Endosulfan has also been found in meat—in Australian beef at levels up to 4 times the MRL (Campoy et al 2001) as a result of cattle consuming cotton waste (Agrow 1996; NRA 2000), and in New Zealand beef exported to Korea as a result of illegal use on cattle to control ticks (Collins 2005). It has also been found in lamb and pork in Spain (Garrido Frenich et al 2006), and in goat and chicken in India (Singh et al 2008b).

Endosulfan has been found in 4.2% of samples of seafood products from Southern China (Guo et al 2007), in cockles, oysters and mussels from coastal lagoons in Ghana (Otchere 2005), mussels in India (GEF IO 2002), and cockles, mussels and fish in Malaysia.

It has also been found in freshwater fish in a number of countries including Australia (Nowak 1990), India (Kole et al 2001; Singh & Singh 2007), USA (Hinck et al 2008), Zambia (Syakalima et al 2006), Benin and Kenya (Pazou et al 2006a, 2006b), Tanzania (Henry & Kishimba 2006), Nigeria (GEF SSA 2002), and Uganda (Kasozi et al 2006). It has been found in all trout sampled from the Great Lakes of USA and Canada (GEF NA 2002), in fish from remote lakes of USA's western National Parks (Ackerman et al 2008), and in estuarine fish in Argentina (Lanfranchi et al 2006). It has been found in farmed prawns in India (Amaranemi 2006), and in shrimps and oysters in Jamaica (GEF CAC 2002).

Endosulfan has been found in honey in Turkey (Erdogrul 2007a), and in 23.4% of beeswax sampled from honeybee colonies in France (Chauzat & Faucon 2007).

It has been found in every sample of wine corks analysed in the USA (Strandberg & Hites 2001), and was the most frequent residue in olives and olive oil sampled in Spain (Guardia Rubio et al 2006). It was recently found in herbal 'drug' materials in Korea (Oh 2007), and in infant formula in Spain (Mezcua et al 2007).

Endosulfan has been found in 22% of samples of cottonseed in Punjab, India (Blossom & Singh 2004); and in cottonseed in Pakistan (Parveen 1993).

It has been found in mustard oil and vegetable oil in India (GEF IO 2002).

Endosulfan has also been found commonly in drinking water, including in the Philippines (Bouman et al 2002), Morocco (El Bakouri et al 2007), India (Shukla et al 2006; Kumari et al 2008; Jayashree & Vasudevan 2007a), Pakistan (Tariq et al 2004), USA (US EPA 2002), the Beijing Guanting reservoir in China (Xue et al 2005; Xue & Xu 2006), Colombia at concentrations of 116.6 *u*g/l (GEF CAC 2002), and in household water supplies in a soy growing area near Cordoba, Argentina (Rulli 2006). Levels of 1.85 *u*g/l were found, in 2003, in water samples from the Selangor River in Malaysia, which is used for drinking purposes (Leong et al 2007).

In Sri Lanka endosulfan has been found throughout the tea ecosystem: in fresh tea leaves (1475 *u*g/kg), made tea (446 *u*g/kg), the soil (1058 *u*g/kg) and water bodies (27 *u*g/kg) (Bishnu et al 2008).

Tobacco

As endosulfan is used on tobacco in some countries, and residues have been found in both tobacco and cigarettes (Papadopoulou-Mourkidou & Milothridou 1990), exposure is also likely to occur through the smoking or chewing of tobacco that has been sprayed with endosulfan.

In utero

Findings of endosulfan and its metabolites in both maternal and umbilical cord sera indicates that these chemicals pass though the placental barrier and the foetus is exposed *in utero* (Torres et al 2006), and this may have critical effects on physical development and cognitive functioning of the child (Shen et al 2007).

Pathak et al (2008) found residues of endosulfan in 60% of pregnant women in their survey in Delhi, with levels of 6.9 *u*g/ml in maternal blood and 5.9 *u*g/ml in cord blood, with the mean values (3.7 and 2.27) indicating a 60% transfer from mothers to newborns. They expressed "great concern" about this high rate of transfer and the consequent effects on the growth and development of the infant.

Carreno et al (2007) said the source of exposure in their study on residues in young men appeared to be consumption of contaminated food, mainly fruit and vegetables or contaminated water; however they also found an association between maternal employment in agriculture during pregnancy and serum levels of endosulfan sulphate in the males aged 18 to 23 years, indicating maternal transfer.

Through breast milk

Endosulfan and its metabolites are commonly found in breast milk (see next section), hence the exposure to the newly born infant is equally common.

In 2003 infants in Bhopal, India were found to be consuming, through breast milk, 8.6 times more endosulfan than the acceptable daily intake levels recommended by the World Health Organization. The mothers were all 'unemployed', and the residues was thought to have occurred as the result of eating contaminated fish and vegetables – 78.9% of 422 vegetables tested in another survey were found to contain endosulfan residues (Sanghi et al 2003).

Health Effects and Poisonings

Absorption and accumulation

Endosulfan is absorbed across the skin and absorption is increased with oils or lotions on the skin, and through cuts. It is also absorbed through the gastrointestinal tract and through inhalation. (ATSDR 2000)

Most published studies on body burdens of organochlorine pesticides have not included endosulfan (Torres et al

2006), but where they have, it is almost without exception found, and it can be assumed that endosulfan is a common human contaminant. It has been found in breast milk, adipose tissue, placental tissue, and umbilical cord blood (Cerrillo et al 2005).

Most of the available studies on the body burden of endosulfan relate to Southern Spain, an area of intensive greenhouse agriculture:

- Carreno et al (2007) found endosulfan or its metabolites in 100% of the blood samples from 220 young males;
- Lopez-Espinosa et al (2008) found endosulfan or its metabolites in 16% of the young boys aged 0-15 years who were sampled;
- Botella et al (2004) found them in 78% of adipose and 96% of serum samples from 200 postmenopausal women;
- Torres et al (2006) found them in maternal adipose tissue and serum and in umbilical cord serum of 61% of 72 women giving birth by caesarean section (only 26% of the adipose samples);
- ATSDR (2000) reports that endosulfan was found in the adipose tissue of 30-40% of children hospitalised in an agricultural region in Spain, assumed to be from repeated dietary exposure;
- other studies from Spain have found endosulfan in female adipose tissue (Hernandez et al 2002; Cerrillo et al 2005, 2006; Ibarluzea et al 2004); in breast milk (Campoy et al 2001; Cerrillo et al 2005); in placenta and umbilical cord blood (Cerrillo et al 2005); and in blood serum (Arrebola et al 2001; Martinez Vidal et al 2002).

In Portugal, endosulfan sulphate was present in the highest mean level and greatest frequency of detection of all organochlorines measured, in blood serum of male and female students, with the mean level in females being even higher than in women in Spain (Lino & da Silveira 2006) with levels up to 1295.5 *u*g/l.

Endosulfan was found in all samples of breast milk from 280 women, and in all placental samples from 130 women, in Denmark and Finland (Damgaard et al 2006; Shen et al 2007, 2008).

Endosulfan and/or its metabolites have been found in breast milk in Egypt (Saleh et al 1996), Madagascar (at 12 *u*g/gm), South Africa (GEF SSA 2002), El Salvador (GEF CAC 2002); in cord blood samples from pregnant Hispanic farm workers in USA (Cooper et al 2001); in serum of men in India (Singh et al 2008b); and in more than 50% of the sera samples from 21 couples in Canada seeking fertilisation assistance (Younglai et al 2002).

In the Asia Pacific region, it has been found in breast milk in Kazakhstan (Lutter et al 1998), India (Sanghi et al 2003: endosulfan levels were higher than any other pesticide), Indonesia (Burke et al 2003), in cotton pickers in Pakistan (GEF IO 2002); and in maternal serum (90%) and umbilical cord tissue (70%) of 32 pregnant women in Japan (Fukata et al 2005). In Indonesia alpha endosulfan was found in 80% of the samples from rural areas, but in none of the samples from urban areas, suggesting exposure was through contact with the spray rather than as residues in food.

A survey of cacao farmers in Nigeria found that 29% of them carried residues of endosulfan with a mean level of 50 *u*g/kg (upper level not given) (Sosan et al 2008)—well above the 1 *u*g/kg level found to cause adverse effects in protein deficient rats.

The only study (Ramesh & Ravi 2003) that could be located in which endosulfan was *not* found when sampled for was from Kasargod District in India where villagers had suffered severe health effects from prolonged aerial spraying of endosulfan of a cashew plantation. However, this study, which was commissioned by the plantation corporation, was later exposed when it was found the blood samples had not in fact been taken from the villagers (Yadav & Jeevan undated). A second study (Saiyed et al 2003) found that 78% of the male children sampled had significant levels of endosulfan in their serum (mean = 7.47 *u*g/l) and these were still significantly higher than a control group 10 months after spraying of endosulfan ceased.

Residues have also been found in the liver, kidney and brain of humans (ATSDR 2000).

Treatment

Suggested treatment of endosulfan poisoning includes a stomach pump, administration of activated charcoal, and control of seizures by use of drugs such as phenobarbitol, diazepam, midazolam, phenytoin or phenobarbitone (ATSDR 2000).

Symptoms and consequences of poisonings

Acute effects

The most prominent signs of acute poisoning by endosulfan are hyperactivity, tremors, decreased respiration, shortness of breath, salivation, and convulsions (ATSDR 2000).

Effects reported as a consequence of occupational inhalation and dermal exposure to endosulfan are primarily neurotoxic: headaches, irritated eyes, malaise, nausea, vomiting, dizziness, confusion, agitation, disorientation, irritability, weakness, shortness of breath and irregular respiration, tachycardia, brachycardia, abdominal discomfort after meals; diarrhoea, impaired consciousness, writhing, muscle twitching, and convulsions (ATSDR 2000; UNEP/FAO 2006a). Effects experienced by 22 people spraying rice and cotton were worse for those who had cuts on their legs from the sharp rice leaves (ATSDR 2000).

Effects of ingestion of endosulfan involve respiratory, cardiovascular, haematological and gastrointestinal systems, as well as the liver and kidney. Symptoms include nausea, gagging, vomiting, headache, dizziness, diarrhoea, agitation, writhing, convulsions, sustained epileptic state, loss of consciousness, cyanosis, shortness

of breath, foaming at the mouth, and noisy breathing (ATSDR 2000).

Clinical signs include elevated haemoglobin and white cell count, decreased blood pressure, hyperglycaemia, metabolic acidosis, kidney failure, liver congestion and fatty degeneration, hypoxia, aspiration pneumonia, clots in pulmonary arteries and aorta, cardiogenic shock, and death (ATSDR 2000). A strong odour of sulphur is reported as characteristic of endosulfan poisoning (Ramaswamy et al 2008).

Severe metabolic acidosis has been reported in a case of unintentional endosulfan poisoning in Turkey (Yavuz et al 2007).

Autopsies have revealed oedema of the brain and lungs, haemorrhage of the medullary layer of the kidney, necrosis of the kidney tubules, acute lung emphysema, congested lungs, inflammation of the stomach and small intestine, and chromatosis of the neurons (ATSDR 2000).

Death has been reported to have occurred from 3 hours to 10 days after ingestion, and has occurred from cardio-respiratory arrest, heart failure, pulmonary oedema, and cerebral hernia from massive cerebral oedema (ATSDR 2000).

Foetal death occurred after a 5-month pregnant woman ingested endosulfan to provoke abortion. A relatively low concentration of endosulfan in the blood of the mother, 470 *u*g/kg, caused relatively quick death of the foetus (Sancewicz-Pach et al 1997).

Long-term effects

Chronic liver and kidney damage may be expected from both short-term high level and long-term low level exposures (ATSDR 2000), as well as a range of other effects.

Neurological

One case of occupational inhalation, in an Israeli chemical factory, led to long-term brain damage with psychiatric manifestations. The man suffered long-term cognitive and emotional deterioration, severe memory impairment, and inability to perform small tasks, with impaired visual-motor coordination. The acute phase included malaise, repeated convulsions and impaired consciousness, and after recovery from these the person became disoriented and agitated (Aleksandrowicz 1979).

In a person who attempted suicide, recurrent convulsions over two weeks were followed by a slow recovery but his mental activity was still severely impaired a year later and he required medication to control seizures (ATSDR 2000).

Acute poisoning symptoms in a teenage girl were followed by psychosis, cortical blindness and limb rigidity (Pradhan et al 1997).

An agricultural pilot exposed to endosulfan showed persistent “nonspecific epileptic foci in the cerebral frontal lobes” (ATSDR 2000).

The ATSDR (2000) concluded that humans with a predisposition to seizure disorders through hereditary or environmental causes may be at increased risk to the adverse effects of endosulfan.

A recent study in California has linked maternal non-occupational exposure to endosulfan and dicofol to autism in children amongst women living within 500m of its application during the first trimester of pregnancy, suggesting exposure by inhalation of drift. The rate of autism was 6 times higher than expected—possibly caused by endosulfan’s interference with GABA-mediated neurotransmission, which plays an important role in gestational brain development. The first 8 weeks of foetal life is the period during which the central nervous system development begins (Roberts et al 2007).

Cancer

The ATSDR (2000) concluded “we do not know whether endosulfan has ever affected the ability of people to fight disease or has ever caused cancer in people”.

One epidemiological study on environmental oestrogens and breast cancer found an increased risk of breast cancer (but not statistically significant) amongst women with elevated adipose tissue levels of endosulfan (in combination with DDE, aldrin and lindane) in a hospital-based case-control study involving 198 cases and 260 controls (Ibarluzea et al 2004).

Reproductive

There have been several reports of adverse reproductive outcomes linked with endosulfan. Rupa et al (1991) found decreased male fertility, increased stillbirths, neonatal deaths and congenital birth defects (such as anencephaly, cleft palate, harelip, club foot, limb malformations, eye deformities and extra fingers or toes), amongst families of those exposed to endosulfan and other pesticides in India’s cotton fields.

Endosulfan was one of 8 organochlorine pesticides measured in significantly higher concentrations in mothers who gave birth to boys with cryptorchidism than in women who gave birth to normal boys, in a study in Denmark and Finland (Damgaard et al 2006). Cryptorchidism has also been linked to endosulfan in southern Spain, where higher rates coincide with intensive use of the insecticide and high rates of residues in children’s adipose tissue (40%) (Saiyed et al 2003).

Chronic effects on male reproductive development were found in villagers in Kasargod, south India exposed to endosulfan, including delayed sexual development (significantly reduced development of pubic hair, testes, and penis) and reduced synthesis of testosterone. These findings correlate with animal studies that show endosulfan inhibits steroidogenesis and spermatogenesis (Den Hond & Schoeters 2006). Additionally, there were six cases of congenital malformations—3 undescended testicles, 3 congenital hydrocele, 1 congenital inguinal hernia—compared with one only (a congenital inguinal hernia) in a comparable less exposed group. Endosulfan was detected in the serum of 78% of the children in the study group and in 29% of the control group, but at a

median level 5.45 times greater than that of the less exposed control group (Saiyed et al 2003).

Other effects noted in Kasargod and attributed to exposure to endosulfan included:

- congenital deformities of hands, feet and heart especially in females;
- other congenital deformities including a child born with her bladder outside her body;
- endometriosis, early menarche, frequent menstrual disorders, male breast enlargement;
- liver cancer, haematological cancers, brain tumours (neuroblastoma);
- congenital mental retardation, cerebral palsy, delayed mental and psychomotor development, learning disabilities, low IQ;
- psychiatric disturbances including committing suicide, epilepsy;
- frequent illness, skin diseases;
- ear nose and throat problems; and
- vision impairment and full loss of vision.

(Quijano 2002; Yadav & Jeevan undated; NIOH 2003; Venugopal 2008).

A survey by the Kasargod District Committee found a disability rate 73% higher than the norm for Kerala State, and the rate of locomotor disability and mental retardation taken together was 107 % higher than the norm (Yadav & Jeevan undated; NIOH 2003).

Cases of Poisonings

Numerous intentional and unintentional deaths have occurred from ingestion of endosulfan, and poisonings are reported for Benin, Colombia, Costa Rica, Cuba, Guatemala, India, Indonesia, Malaysia, Philippines, New Zealand, South Africa, Sri Lanka, Sudan, Turkey and USA. It is regarded as one of the main causes of poisoning in many countries (Kishi 2002) including in Asian countries (Roberts et al 2004), Turkey (Oktay et al 2003), Latin America (Wesseling et al 2005), and West Africa (Glin et al 2006).

Intentional

An analysis of poisonings from pesticides in the Warangal district of Andhra Pradesh, India during 1997 to 2002, revealed that endosulfan and monocrotophos caused the majority of the 1,817 deaths (8040 hospital admissions for pesticides with a 22.6% fatality rate). 96% of these hospital admissions were intentional poisonings (Srinivas Rao et al 2005). Such deaths are still continuing with one of the most recently reported being that of a 26 year-old woman in Chandigarh (Ramaswamy et al 2008).

In 2005, 17 males were admitted to just one hospital in Turkey, that of Ondokuz Mayis University in Samsun, after ingesting endosulfan (Karatas et al 2006).

According to Roberts et al (2003), in Sri Lanka the replacement of banned organophosphates by endosulfan after 1995 led to a rise in deaths from endosulfan poisoning, from 1 in 1994 to 50 in 1998. At this point endosulfan was also banned and deaths from it fell to 3 over the following 3 years. Gunnell et al (2007) reported that, following the Sri Lankan restrictions on WHO Class I pesticides in 1995 and endosulfan in 1998, the rate of self-poisoning fell significantly with 19,769 fewer suicides in 1996–2005 as compared with 1986–95. No other trends appeared to be associated with this decline.

In Malaysia, 15 endosulfan poisoning incidents were recorded for the years 1987 and 1988, but whether they were intentional or not is not reported (Arumugam 1992).

Unintentional

According to GFEA-U (2007), endosulfan is one of the most frequently reported causes of poisoning globally. It has caused congenital physical disorders, mental retardation and death in farmer workers and villagers in Africa, southern Asia and Latin America.

Asia

Philippines

In 1991 endosulfan accounted for the largest number of pesticide poisonings reported to the National Poisons Control and Information Centre, and continued to be one of the main causes of poisoning until it was banned (Quijano 2000).

Indonesia

A number of poisonings have occurred in Indonesia: in southern Sulawesi it was the leading cause of pesticide poisoning between 1990 and 1993, responsible for 32 of 153 reported poisoning cases (ERMANZ 2007b).

India

In Haryana accidental exposure during spraying of endosulfan (18 cases) accounted for one third of the total number of poisoning cases admitted to the Post Graduate Institute of Medical Sciences between October 1995 and September 1997 (Chugh et al 1998).

Repeated episodes of convulsions in 36 people from a number of families in a rural area of Jabalpur District in Madhya Pradesh was eventually traced back to food unintentionally contaminated with endosulfan. One of the food items consumed was laddu prepared from wheat flour contaminated with 676,000 *u*g/kg of alpha endosulfan. The exact cause of the contamination was not confirmed but suspected to be from reuse of endosulfan containers for food storage (Dewan et al 2004).

At a rural roadside food stall a half-filled bottle of endosulfan, without its lid, was stored on a shelf. It fell into the wet flour used to make idlis. Forty-four people consumed idli and tea. They experienced nausea, vomiting altered senses, seizures, diarrhoea, and abdominal pain. One died of asphyxia. Two people remained unconscious for 24 hours, and 30 remained unconscious for up to 18 hours (Venkateswarlu et al 2000).

The village of Kasargod in Kerala, India, experienced sustained exposure to endosulfan as a result of 20 years of aerial spraying of a nearby cashew nut plantation. Endosulfan was the only pesticide used. Twelve streams used by the villagers originated in the plantation and were

subsequently found to have contaminated sediment and water throughout the year (outside the spray season), as a result of endosulfan's persistence in soil and the soil being carried to the streams by storm runoff. Residues were still detected in the water and pond sediments 1.5 years after spraying ceased (Saiyed et al 2003). One sample contained endosulfan at 391 times the maximum permissible level (Kumar 2002). The villagers were also directly exposed to spray drift. Numerous congenital, reproductive, long term neurological and other symptoms were experienced (see previous section). 197 cases were documented from just 123 households. Chronic morbidity was 70% higher than the norm. There were observations of similar effects in animals too: cows giving birth to deformed calves, cows and chickens dying inexplicably, domestic animals with miscarriages, bleeding, infertility, stunting of growth and deformities, as well as fish kills and dwindling populations of honeybees frogs, and birds (Quijano 2002; Yadav & Jeevan undated; NIOH 2003). Endosulfan has subsequently been banned in the State of Kerala and compensation paid to some of the victims and/or their families by the State (Venugopal 2006). The families of at least 135 victims who have died have received compensation (Venugopal 2008).

A massive effort, by the Kerala State Government, is now underway to provide treatment for the victims. Approximately 2000 are registered, and so far treatment has been provided for 153 victims with ear, nose and throat ailments, 162 with impaired vision, 103 who lost vision fully or partially, as well as other surgeries (Venugopal 2008).

Africa

Endosulfan had been removed from West African cotton growing because of its high toxicity, but it was re-introduced in 1998-1999 in Mali and Benin, and in 1999-2000 in Senegal, Cameroon and Burkina Faso to control *Helicoverpa,* the cotton bollworm, which had become resistant to pyrethroids. Poisonings soon became apparent, particularly in Benin (Ton et al 2000).

Benin
The poisonings were unintentional and occurred as a result of exposure in the cotton fields. At least 37 people are known to have died in the 1999/2000 season, with an estimated total death toll of 70 and with another at least 90 people suffering illness. The figures are considered a significant underestimation because of lack of adequate reporting. Deaths and poisonings were reported in 16 villages in 7 out of 12 districts in the Borgou province alone (Ton 2000; Ton et al 2000). A separate study (the OBEPAB study) of the Bourgou region for that season found that endosulfan was responsible for 60% of poisonings (Ton et al 2000). Over the years 2000-2003, endosulfan caused 400 poisonings in Benin, of which 347 were fatal, accounting for 69% of all pesticide poisonings in that country; food contamination was the main problem (Glin et al 2006).

"On August, 24, 1999, in the village of Maregourou, three boys between the age of 12 to 14 went to weed the cotton field of their father. The cotton crop was cultivated together with maize. The day before, the father had sprayed the field with endosulfan and the boys did not know. After the work, they were hungry and they took a few maize cobs to eat. Fifteen minutes later they started vomiting. They were taken to the hospital of Bembereke where one boy of 12 died. The two others survived." (Ton et al 2000).

Senegal
A range of surveys carried out by PAN Africa 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 all the 162 poisonings, including 20 deaths, 73.2% occurred from exposure during application (Glin et al 2006).

Mali
A survey by PAN Africa in 2001, of 178 people in 21 villages in Kita, Fana and Koutiala, found 73 cases of poisoning. Endosulfan was the main insecticide used (Glin et al 2006).

Togo
Preliminary studies carried out by ANCE-Togo, in 2003, indicated that there were more than 500 cases of poisonings related to the use of endosulfan registered each year with the Division of Toxicology of the public hospital of Lomé-Tokoin (Kodjo 2007).

Sudan
In Sudan 12 of the 17 reported insecticide poisoning incidents between 1981 and 1991 involved endosulfan. In 1981 3 out of 4 people poisoned by endosulfan in Gedarif died. In 1993 there were 100 poisonings with no deaths in Rufaa. The worst recorded case was 250 poisonings with 31 deaths in Alabaydia in 1991, with another 13 poisonings in Dongola in the same year. In all there were at least 402 poisonings and 46 deaths from 1981 to 1991. However the number is likely to be substantially larger than this because no figures are reported for 6 of the 12 incidents and many incidents may not have been reported. Most of the poisonings were thought to occur from contaminated food (El Hindi et al 2006). Not included in these figures were the deaths of 31 people in 1988 from eating seeds treated with endosulfan (Glin et al 2006). In that year another 3 people died after drinking water from a canal in which empty endosulfan drums had been washed (Glin et al 2006).

South Africa
In South Africa two children died in 2003 after coming into direct contact with a goat that had been treated with endosulfan (endosulfan was sold as a veterinary vaccination) (Glin et al 2006).

Latin America

Endosulfan is one of the main culprits of pesticide poisoning in Central America (Wesseling et al 2005).

In the most recently reported case, one farmer died and 154 others were poisoned by endosulfan used to protect coffee and banana crops in the central western Quindio province of Colombia–despite endosulfan having been banned in Colombia since 2001 (Mingxin 2007).

Previously, 60 poisonings and one death were reported in 1993 due to endosulfan use on coffee in Colombia; and in 1994 Colombia's Departmental Committee of Coffee Growers recorded 155 cases of pesticide poisoning, most of which were due to endosulfan (EJF 2002). In Guatemala there were 26 poisonings by endosulfan in 1999 (GEF CAC 2002). In El Salvador the vast majority of the 150 poisonings reported between 1998-2000 were caused by endosulfan; there were another 60 cases of endosulfan poisoning in 2000 and 20 in 2001. A smaller number is reported for Honduras, and 15 in Costa Rica for 1993 to 2001 inclusive. In Cuba, 15 people died after consuming fritters, accidentally contaminated with endosulfan, from a street vendor (PANNA 1999).

Other countries

New Zealand
Three cases of unintentional exposure have been reported—with symptoms including swelling, sore nose, blistered lips, nausea, abdominal pain, sweating and vomiting—and one case of intentional exposure (ERMANZ 2007b).

USA
In 2001 a schoolgirl in Wenatchee, Washington was affected by endosulfan that had drifted from a nearby apple orchard. She was in a stupor, eyes rolled back in her head, unable to speak, and with an abnormally fast heart rate. Investigators found her clothes soaked with endosulfan picked up from residues on the grass of the schoolyard and subsequently absorbed into her bloodstream (Associated Press 2007).

Environmental Effects

"Endosulfan is very toxic to nearly all kinds of organisms" (GFEA-U 2007).

Aquatic toxicity

Endosulfan is extremely toxic to fish and its use results in the disruption of the aquatic food chain. It is especially toxic to juveniles (Dutta & Arends 2003).

In fish it causes marked changes in sodium and potassium concentrations, decreases in blood calcium and magnesium levels, inhibits brain ATPase, and can cause massive fish kills (Naqvi & Vaishnavi 1993). It inhibits acetylcholinesterase in the brain of fish (Dutta & Arends 2003).

Endosulfan also has the capacity to have chronic effects on aquatic organisms—as reported earlier it has recently been found to be genotoxic to freshwater fish, causing single-cell DNA strand breaks in tissue of the gill, kidney and erythrocytes (Sharma et al 2007a). It was also found to be genotoxic and embryotoxic to Pacific oysters and, as embryotoxicity governs recruitment rate, it is therefore likely to adversely affect population dynamics at sublethal concentrations (Wessel et al 2007).

Bollmohr et al (2007) established a range of figures to identify hazardous concentrations of endosulfan in freshwater and marine systems. HC5 (*u*g/l) = the hazardous concentration of total endosulfan which affects 5% of freshwater ($HC5_{freshwater}$) and marine organisms ($HC5_{marine}$):

$HC5_{freshwater}$
- arthropods = 0.02 *u*g/l
- fish = 0.05 *u*g/l
- mean freshwater = 0.03 *u*g/l

$HC5_{marine}$
- arthropods = 0.02 *u*g/l
- fish = 0.06 *u*g/l
- mean marine = 0.02 *u*g/l

Concentrations of endosulfan found in many rivers, particularly after rainfall events carrying runoff into the rivers, greatly exceed these figures (refer section on surface waters and sediment contamination). Levels of 0.3 *u*g/l are likely to cause fish kills (GEF SEA SP 2002). Investigations in both Australia and East Java indicated that the presence of endosulfan residues was closely associated with the depletion of aquatic biota.

In terms of the toxicity of endosulfan in sediment to aquatic organisms, the US EPA (2007d) identified No Observed Adverse Effects Concentrations (NOAECs) of 480 to 860 *u*g/kg of sediment for aquatic invertebrates. Levels of up to 626 *u*g/kg have been found in the sediment in dams in South Africa (Dalvie et al 2003).

The US EPA (2007d) described endosulfan as *very highly toxic* to all aquatic organisms, as demonstrated by the low concentration of endosulfan that kills 50% of a species (LC_{50}) after 48 or 96 hours of exposure, and the low NOAECs:

LC_{50} (96 hr) as *u*g/l:
- rainbow trout = 0.8
- bluegill sunfish = 1.7
- fathead minnows = 1.5
- striped bass = 0.1
- eastern oyster = 0.45
- grass shrimp = 1.3

LC_{50} (48hr) as *u*g/l:
- scud (shrimp-like crustacean) = 6
- water flea (Daphnia) = 199

NOAEC (*u*g/l):
- rainbow trout = 0.1
- fathead minnows = 0.2
- scud = 0.07
- water flea = 2.0
- striped bass = 0.01
- eastern oyster = 0.05

However Leonard et al (2001) reported an LC_{50} for mayfly in the Naomi River, Australia, as 0.7 *u*g/l for beta endosulfan and 1.2 *u*g/l for endosulfan sulphate—considerably less than those proposed (above) by the US EPA (2007d) for aquatic invertebrates, and considerably less than measured concentrations in river water following storm run-off in several countries.

Fish
Chronic effects on fish, including physiological, ethological and morphological effects have been reported at

concentrations ranging from 0.5 to 5 *u*g/l (GFEA-U 2007). Sublethal exposure to endosulfan causes oxidative damage in the brain (Ballesteros et al 2008); and alters acetyl cholinesterase activity in the brain resulting in changes in growth, survival, feeding, and reproductive behaviours (Dutta & Arends 2003). It induces changes in the levels of circulating thyroid hormones (Sinha et al 1991a, 1991b), structure of the thyroid gland (Park et al 2004), and in peripheral thyroid hormone metabolism, the nature of which differs between tissues (Coimbra et al 2005). In exposed embryos it altered the distribution of primordial germ cells, which may affect the structure and function of gonads (Willey & Krone 2001). It caused damage to testes of male fish—including to the Leydig cells, Sertoli cells, and seminiferous tubules—that is likely to have a negative effect on male fertility (Dutta et al 2006). Significantly lowered levels of testosterone and oestradiol have been found in fish with elevated residues of endosulfan (Singh et al 2008b). They also found that the preferential order of bioaccumulation of endosulfan in fish was ovary > liver > brain > blood, indicating vulnerability to reproductive dysfunction. When fish eggs were exposed to sublethal endosulfan, it delayed their hatching, and resulted in decreased number and growth of fry, which upon reaching maturity also produced fewer eggs and these took longer to hatch, demonstrating a transgenerational effect (Gormley & Teather 2003). It has been shown to be genotoxic in gilthead seabream (Neuparth et al 2006).

There is evidence of transgenerational transfer of endosulfan in fish, with changes in offspring and reproductive ability recorded over two generations of rainbow trout. Fertility and hatch rates were significantly reduced, after suspected parental transfer of endosulfan to embryos, indicating the potential for a significant impact on endosulfan-exposed populations (Holdway et al 2008).

Exposure to sublethal concentrations of endosulfan caused significant reduction in the upper critical temperature tolerance of freshwater fish in Australia (Patra et al 2007), a significant concern in light of climate change. Similarly freshwater fish were able to survive higher concentrations of endosulfan at lower water temperatures (Capkin et al 2006). A similar response was found with the eggs and larvae of the bollworm: higher temperatures and higher humidity increased the toxicity of endosulfan (Satpute et al 2007).

Crustaceans

With freshwater prawns exposure to endosulfan caused fast jerking, frequent jumping, erratic swimming, spiralling, convulsions, tendency to escape from aquaria, secretion of mucus over the gill area, and severely impaired growth (Montagna & Collins 2007). Sublethal exposures damage the gills (Selvakumar et al 2005).

Shrimps are also very sensitive to endosulfan and inflow into aquatic areas is likely to adversely affect shrimp production (Casto-Castro et al 2005). Sublethal concentrations can reduce the rate of reproduction (Wirth et al 2002).

At sublethal concentrations endosulfan also disrupts lipid metabolism, cell function and energy production necessary for maintaining physiological processes in freshwater field crabs that inhabit paddy fields in India (Rafi et al 1991; Reddy et al 1992). These crabs are regarded as of high importance as food for rural populations (Reddy et al 1992). Endosulfan is known to interfere with enzymes crucial to the moulting process of crabs (Zou & Fingerman 1999). It has also been found to increase the duration of the moulting period in mangrove crab potentially reducing its success in reaching adult stage (Kannupandi et al 2001).

Aquatic invertebrates

In aquatic invertebrates, endosulfan causes deceases in adenylate energy charge, oxygen consumption, haemolymph amino acids, succinate dehydrogenase, heartbeat (in mussels), and altered osmoregulation (Naqvi & Vaisnavi 1993), as well as causing impairment of feeding, growth rates, embryonic development and reproduction rate (GFEA-U 2007).

A NOEC of 100 *u*g/l for feeding efficiency has been reported for *Daphnia magna. Daphnia* readily accumulates endosulfan from the surrounding water, particularly the beta isomer. It has also been shown to affect growth and reproduction of *Daphnia* (DeLorenzo et al 2002), and to inhibit moulting (Zou & Fingerman 1997).

The metabolite, endosulfan sulphate, also interferes with reproduction in *Daphnia*, causing a significant decrease in number of offspring, with reduced size of females and an increased proportion of males. It causes a decrease in moulting frequency, early development arrest, and a range of embryo deformities, including underdeveloped second antennae, curved, incurved or non-existent shell spine and other morphological alterations of the carapace.

The concentrations of endosulfan sulphate that affect reproductive outcome are significantly lower than for similar effects caused by endosulfan isomers (9.20 *u*g/l compared with 120 *u*g/l) (Palma et al 2008).

A small water flea (*Moina macrocopa*) that is widely distributed in ponds and rice fields in Southeast Asia is also affected by endosulfan at low concentrations. At 2 *u*g/l, longevity, initial age of reproduction and intrinsic rate of natural increase were reduced, and at 0.4 *u*g/l there was a 70% reduction in fecundity. Zooplankton such as this water flea are an important link in the aquatic food chain so effects on these populations have flow on effects on their larger prey resulting in changes at community and ecosystem level (Chuah et al 2007).

Endosulfan caused significant decreases in populations of dragonflies and mayflies in streams in Argentina, following rainfall events that caused runoff from soy fields (Jergentz et al 2004). Levels were detected in suspended particles of up to 318 *u*g/kg.

Effects of endosulfan on freshwater invertebrates indicate that endosulfan use on rice fields in Portugal may be causing ecological imbalance in nearby freshwater wetlands (Faria et al 2007).

A study of macroinvertebrate populations indicated that endosulfan is the likely cause of changes observed in Australian river systems in cotton-growing areas (Hose et al 2003). Mayflies were most affected by the endosulfan, and algal blooms followed the disruption to the insect populations.

Amphibians

Sublethal concentrations of endosulfan reduced survival of tadpoles by increasing their vulnerability to predation, and especially so when water temperatures were elevated (Broomhall 2002). It also reduced their size and feeding behaviour (Broomhall & Shine 2003). Endosulfan has been implicated in the decline of frog populations in California, possibly by depressing acetylcholinesterase activity in tadpoles (Sparling et al 2001).

Concentrations as low as 430 *u*g/l, significantly lower than those commonly found in ponds and streams near agricultural fields, killed 50% of the tadpoles of the common toad *Bufo bufo*. Additionally sublethal concentrations damaged the structure and function of the tadpole gills (Bernabo et al 2008).

Non-toxic concentrations of endosulfan interfere with the pheromone systems of both male and female newts, disrupting mate selection and causing reduced mating success (Park et al 2001; Park & Propper 2002).

Sublethal concentrations also affect salamanders—causing reduced larval survival and activity, reduced growth, limb deformities and respiratory distress (Rohr et al 2003).

Reptiles

Exposure of eggs of a South American caiman (similar to alligators) to endosulfan caused loss of egg weight and reduced weight in the hatchlings, thought to be as a result of disrupting the metabolism of the embryo and the signals that control development (Beldomenico et al 2007).

Endosulfan sulphate inhibited progesterone receptor binding in alligators, interfering with the functioning of progesterone (Vonier et al 1996).

Snails

Freshwater snails, and especially the newly emerged juveniles are highly susceptible to endosulfan, particularly to longer exposures, and persistent or continuous residues in water are likely to drastically affect snail communities (Oliveira-Filho et al 2005). Sublethal concentrations caused adverse effects in the digestive gland, foot and mantle of the great ramshorn snail common in Europe in small temporary ponds and streams (Otludil et al 2004).

Aquatic plants

Endosulfan reduced productivity in a phytoplankton community by 86.6% during a four-hour exposure period (IPCS 1984).

A NOEC of 130 *u*g/l has been reported for growth of the freshwater green algae *Pseudokirchneriella subcapitatum.* The algae readily accumulate endosulfan from surrounding water, particularly the alpha isomer. It has been shown to impair growth and have chronic reproductive effects in marine red algae (DeLorenzo et al 2002).

Endosulfan induces oxidative stress, an indicator of sublethal stress, in the aquatic macrophyte *Myriophyllum quitense* (water milfoil) (Menone et al 2008); and genotoxicity in the wetland macrophyte *Bidens laevis* L (bur marigold, or beggars tick) (Perez et al 2007)—at environmentally relevant concentrations of 5 *u*g/l.

Coral Reefs

Coral organisms are highly sensitive to endosulfan at around detection limits, with effects noted including bleaching, reduced larval set, metamorphosis and photosynthetic efficiency. Contamination of coral reefs with run-off from agricultural areas could have a profound effect—even at levels at the limits of detection—on the replenishment of populations of coral organisms, and hence survival of the reefs (Markey et al 2007).

Terrestrial ecotoxicity

Birds

Endosulfan is highly toxic to birds:

- Acute LD50: 28,000 *u*g/kg (mallard duck)
- Dietary (5 day LC50): 805,000 *u*g/kg (Northern bobwhite quail) (US EPA 2007d)

Endosulfan is immunosuppressive in bird species (Bhattacharya et al 1993; Kurkure et al 1993; Khurana & Chauhan 1998; Garg et al 2004). Exposure of chicken eggs to extremely low doses of endosulfan (2 *u*g) results in adverse effects on the liver and brain enzymes, decreased DNA and RNA in the brain, and immunosuppression (reduction in IgG content and lymphocyte count, and changes in the lymphoid organs) (Pushpanjali et al 2005). Exposure of chickens to sublethal doses of endosulfan has adverse effects on metabolism (Garg et al 2004).

Bees

Endosulfan is highly toxic to bees:

- LD_{50} (96 hrs) = 4,500 *u*g/kg (US EPA 2007d)
- Acute oral toxicity LD_{50} = 2 *u*g ai/bee (based on formulation product) (UNEP/FAO 2006b)
- Acute contact toxicity LD_{50} = 0.82 *u*g ai/bee (based on formulation product) (UNEP/FAO 2006b)

Sublethal effects of endosulfan include reduced olfactory learning (Decourtye et al 2005).

Soil micro-organisms

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). Actinomycetes are beneficial bacteria that play a vital role in replenishing the supply of nutrients in the soil: they help with the decomposition of organic matter and the formation of humus, particularly by breaking down cellulose and chitin. They also help non-leguminous plants fix nitrogen.

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).

Earthworms

- LC_{50} = 1,500 *u*g/l in the species *Pheretima posthuma* (Hans et al 1990)
- LC_{50} (15 days) = 3,360 *u*g/l in *Lumbricus terrestris* (Mosleh et al 2003)
- LC_{50} (15 days) (endosulfan sulphate) = 51,500 *u*g/kg (UNEP/FAO 2006b)

Endosulfan is highly toxic to earthworms, especially juveniles (Awaknavar & Karabhantanal 2004), hence its use in New Zealand to kill earthworms in turf. Of 5 pesticides (endosulfan, dicofol, carbofuran, carbendazim, trifluralin) tested on earthworms, endosulfan was by far the most toxic, killing 100% of *Lampito mauritii* (Mahanthaswamy & Patil 2003).

At concentrations of 10,000 *u*g/kg of earth endosulfan caused swollen body, excessive mucus, sluggish movement and, at 100,000 *u*g/kg, it caused instant death (Hans et al 1990). Other sublethal effects include reduced growth rate (Mosleh et al 2003), and reduced reproduction (Awaknavar & Karabhantanal 2004). So-called 'normal' application rates significantly reduced the weight and cocoon production of *Aporrectodea trapezoids,* and it was concluded that normal use of endosulfan could significantly reduce populations of earthworms in agricultural soils (Choo & Baker 1998).

Beneficial insects and fungi

Endosulfan is highly toxic to beneficial insects, and it is not compatible with IPM programmes.

It significantly reduced the emergence and the parasitism of the parasitic wasp *Trichogramma pretiosum* (Bastos et al 2006), which kills the eggs of various moth pests such as heliothis, corn borer, cabbage moth, loopers, and yellow peach moth.

It is toxic to *Orius insidiosus* (Minute pirate bug / insidious flower bug), which predates thrips, mites, aphids and small caterpillars; and to the parasitic wasp *Aphidius colemani*, which parasitizes aphids (Bostanian & Akalach 2004)—both important in glasshouse IPM programmes.

Orius insidiosus also predates *Helicoverpa zea*, cotton bollworm, as does *Geocoris punctipes*. Endosulfan is toxic to both of these predators, but more so to females of the latter species, and it reduces fecundity and consumption of bollworm eggs by both predators (Elzen 2001).

It is also toxic to the predacious mite *Phytoseiulus persimilis*, which predates upon spider mites and is very important in IPM programmes. Endosulfan reduces the number of females laying eggs and the number of eggs that hatch (Bostanian & Akalach 2006).

Endosulfan is highly toxic to the eggs and larvae of *Chrysoperla externa*, a lacewing that predates mites and so is a valuable biological control species (Schneider et al 2006).

It also reduces prey consumption and web building of the spider *Araneus pratensis*, an important predator of agricultural pests such as midges, and an indicator of ecosystem disturbance (Benamú et al 2007).

Endosulfan significantly reduced the development of the 'entomopathogenic' fungus, *Verticillium lecanii* (Zimm.)—a fungus used in some IPM programmes to kill insect pests such as aphids, thrips and whitefly (Alizadeh et al 2007).

Plants

Toxic effects on plants include altered permeability of root membranes resulting in coiling of the root radical, inhibition of root growth, stunting of shoots, and burning of the margins and tips of leaves (IPCS 1984).

Environmental fate

Persistence

In soil

Endosulfan is persistent in the soil. The Stockholm Convention on Persistent Organic Pollutants (POPs) defines persistence as having a half-life (DT_{50}) in soil of > 183 days.

Endosulfan is oxidised in plants and soil by microbial action to form endosulfan sulphate, and by hydrolysis to form endosulfan-diol.

Aerobic conditions

- alpha endosulfan DT_{50} = 12-39 days (mean = 27.5)
- beta endosulfan DT_{50} = 108-264 days (mean 157)
- total endosulfan DT_{50} = 288-2,241 days, or 9 months to 6 years (GFEA-U 2007); 1,336 days (US EPA 2007c)

Anaerobic conditions

These are expected to considerably extend the half-lives in soil (GFEA-U 2007).

Tropical soils

DT_{50} total endosulfan in Brazil was 161-385 days, i.e. it is less persistent in tropical soils.

In water

The half-life in water varies from 35-187 days under anaerobic conditions (ATSDR 2000). The Stockholm Convention regards a chemical as being persistent in water if its half-life is > 2 months: endosulfan is persistent in water under some conditions.

Increasing pH increases hydrolytic breakdown of endosulfan, which is the main degradation process in seawater, thus endosulfan is more persistent in acidic conditions (GFEA-U 2007):

- At 25 °C, DT_{50} at pH 7 is 10-20 days, and at pH 9 it is 0.2 days (GFEA-U 2007).
- In seawater, which is alkaline, the half-life of alpha endosulfan was 22 days, and of beta endosulfan 8.3 days (GFEA-U 2007).

The half-life in a water/sediment microcosm in a Brazilian wetland was measured as up to 63.6 days (DT_{50}) for beta endosulfan and 20.4 for alpha endosulfan (Laabs et al 2007).

In plants

The estimated half-life of endosulfan in cotton plant material in Australia is 65 days (Kennedy et al 2001). One study on rice in India found that foliar concentrations of alpha endosulfan initially of 48,400 *u*g/kg reduced to 13,300 *u*g/kg after 75 days, but were still present at 7,400 *u*g/kg after 225 days. The rice at harvest contained 2,200 *u*g/kg endosulfan sulphate (Jayashree & Vasudevan 2007b).

Bioaccumulation, bioconcentration, and biomagnification

Bioaccumulation is a general term for the accumulation of substances in an organism through respiration, food intake, absorption through the skin, etc, resulting in the organism having a higher concentration of the substance than the concentration in the surrounding environment.

Bioconcentration is bioaccumulation that occurs when uptake is from water only; the octanol-water partition coefficient (K_{OW}) of the substance is used to determine its ability to bioaccumulate.

Biomagnification is the bioaccumulation of a substance up the food chain, and it can result in higher concentrations of the substance than would be expected if water were the only exposure mechanism. The biomagnification factor (BMF) is the ratio of the concentration of the chemical in the organism to the concentration in its food, and biomagnification occurs if the ratio is >1.

The Stockholm Convention (and the US) recognises a chemical as bioaccumulative if it has a bioaccumulation or bioconcentration factor (BCF) > 5,000 in an aquatic species, or a log K_{ow}>5. The EU recognizes bioaccumulation when the BCF is $\geq$ 2000 (Kelly et al 2007).

Estimates of log K_{ow} (GFEA-U 2007):
- alpha endosulfan = 4.65
- beta endosulfan = 4.34
- endosulfan sulphate = 3.77

The US EPA (2007d) put the range of log K_{ow} for the 3 forms of endosulfan as 3.55-4.78.

Alpha endosulfan is more bioaccumulative than the beta isomer or the sulphate.

The measured BCF in aquatic organisms covers a wide range:
- oysters and bivalves = < 100
- whole fish, fresh and marine = 2,400 to 11,000
- freshwater green algae = 2,682
- *Daphnia* = 3,278

(DeLorenzo et al 2002; GFEA-U 2007)

The highest BCF was for the fish yellow tetra, with a value of 10,994 for the alpha isomer, 9,908 for the beta isomer and 11,583 for both isomers together (Jonsson & Toledo 1993). These figures are well above the Stockholm Convention requirement of 5,000.

The US EPA (2007d) estimated a BCF range of 1000 to 3000.

DeLorenzo et al (2002) noted that the BCF of 3,278 for *Daphnia* is similar to those reported for the POPs pesticides DDT, dieldrin and chlordane of 2,500-12,000. They also noted that this BCF of 3,278 was for neonates and it is expected to be higher for adult *Daphnia*, which have a nearly five times higher lipid content. US EPA (2007d), however, concluded a range of 20-600 for aquatic invertebrates.

The US EPA (2002) considered endosulfan to have a high potential to bioaccumulate in fish, and hence may affect animals higher in the food chain. However US EPA (2007d) reported a calculated BMF in aquatic organisms as up to 1.38 for piscivorous fish and regarded it as not significant.

Even if the threshold of 5,000 for a BCF for aquatic species is not met, the Stockholm Convention accepts other evidence of bioaccumulation—in particuar evidence of high bioaccumulation in other species, or "monitoring data in biota indicating that the bioaccumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention". Such evidence certainly exists.

Vorkamp et al (2007) found endosulfan residues in every single species, both terrestrial and aquatic, that they tested in Greenland (see section on Contamination of biota, p27 for details). The authors reported that, whilst there was significant accumulation of endosulfan in tissue, and some evidence of biomagnification in fish (wolfish and caplin), there did not appear to be appreciable biomagnification higher up in the aquatic food chain as levels in fish eaters were generally not higher than in fish.

However, Kelly & Gobas (2003) and Kelly et al (2007) have proposed that the biomagnification of endosulfan (particularly the beta isomer) is greater in the terrestrial food chain that the marine food chain, because it has a high log K_{oa} (octanol-air partition coefficient), which is of greater importance than the K_{ow} in air-breathing animals. A high K_{oa} causes slow respiratory elimination.
- log K_{oa} alpha endosulfan =10.29
- log K_{oa} beta endosulfan =10.29
- log K_{oa} endosulfan sulphate =5.18

Armitage & Gobas et al (2008) concluded that chemicals with a log K_{ow} between 1.75 and 12, and a log K_{oa} > 5.25 have the potential to bioaccumulate in air-breathing organisms, hence endosulfan clearly has the potential to biomagnify in terrestrial animals.

Kelly et al (2007) summarised residues of endosulfan found in the Artic food web in Hudson's Bay 1999-2002 to illustrate bioaccumulation (units are ug/kg lipid equivalent, geometric means), especially of beta endosulfan in beluga, a small arctic whale that feeds mainly on fish:

		alpha	beta	sulphate
lichen	-	0.03	-	
sediment	0.16	0.33	0.16	
cod (B. saida)	-	2.91	-	
salmon	0.41	0.85	0.18	
beluga (m)	-	12.56	0.86	
beluga (f)	-	4.87	0.58	
ringed seals (f)		3.02	0.19	
ringed seals (m)	0.30	2.26	0.32	
eider ducks	2.32	-	-	
scoters	-	-	0.87	

Kelly & Gobas (2003) established the following predicted BMFs for beta endosulfan in male wolves at various ages, showing significantly higher biomagnification than found in the aquatic food chain (see preceding paragraph), even at a 1.5 years, and increasing considerably with age:

1.5 years	2.25 years	13.1 years
5.3	*17.9*	*39.8*

Kelly et al (2007) calculated BMFs for endosulfan ranging from 2.5 to 28 for different herbivorous and carnivorous terrestrial organisms. US EPA (2007d) calculated a BMF of 7 for male beluga and 3 for female beluga.

These figures clearly show that endosulfan has the potential to significantly biomagnify in the food chain, and findings of widespread contamination in the Arctic region, with levels increasing over time, support this. Bioaccumulation is occurring even in the aquatic food chain despite some analyses not indicating this.

Braune et al (2005) reported that over 20 years monitoring of POPs in the Canadian Arctic, there was a 3-fold increase in age-adjusted concentrations of endosulfan sulphate in beluga at the same time as most other POPs were declining. Similarly, Evans et al (2005) reported increasing residues of endosulfan in the freshwater fish char—they were 2.2 times higher in 2002 than 1992.

Bioaccumulation is also occurring in non-polar regions. Menone et al (2000) found residues of endosulfan sulphate in the liver, gonads, fat and muscle of fish from a coastal lagoon in Argentina, at levels ranging up to 0.018 *u*g/kg of tissue. They calculated a BMF of 4.02, higher than that for DDT. Lanfranchi et al (2006) found endosulfan biomagnified in striped weakfish also in Argentina. In Zimbabwe, endosulfan was found to accumulate in the tissues of wild rats feeding in to soya bean fields to which endosulfan was applied (Kuvarega & Taru 2007). Levels in liver were generally higher (0.36-5.8 *u*g/kg) than those in muscles (0.09-5.17) and fatty tissues (0.08-4.78 *u*g/kg).

Measurements taken in Ghana indicate that bioconcentration may be occurring in freshwater fish there, according to Darko et al (2008): endosulfan levels in fish (up to 0.42 *u*g/kg) were, on average, 10 times those found in water samples, although the mean level in the sediments was about 14 times the levels measured in fish.

Bioaccumulation has even been found in plants: a BCF of 30.9 was found for endosulfan sulphate in bulrushes from a lake in Argentina, which appear to have sequestered it from the sediment (Miglioranza et al 2004b). This BCF was significantly higher than those for other POPs such as DDT (1.1), chlordane (2.1), dieldrin (2.1), and heptachlor (3.8), with the exception of HCH (61.1).

An analysis of airborne pollutants in the western national parks of the USA, carried out from 2002 to 2007, found evidence of the bioaccumulation of endosulfan in vegetation, the degree of accumulation increasing with forest productivity and proximity to sources of endosulfan. The mean level of total endosulfan in two-year-old needles of White Fir (7573 *u*g/kg lipid) was 3 times higher than the levels in one-year-old needles (2448 *u*g/kg). The degree of bioaccumulation varies between species with firs accumulating substantially higher concentrations than pines. The coniferous forests of the western USA and Alaksa are estimated to be removing between 1,280 and 7,210 kgs of endosulfan from the air annually, amounting to about 2% of the USA's annual usage (Landers et al 2008). There was no estimation of how much other vegetation types might also be accumulating, but there were signficantly higher levels of endosulfan in some lichen species than in the conifers (nearly 6 times higher).

Wang et al (2007a) found that the bioconcentration factor (BCF) of grass for POPs increased with increasing elevation, "indicating that the cold condensation of POPs at high-elevation sites may increase the potential threat to vegetation and the food chain in the mountain ecosystem".

Atmospheric Transport and Deposition

The potential for atmospheric transport of endosulfan is indicated by:

- its ability to volatilise from soil and plants;
- its atmospheric half-life; and
- its ability to interchange between air and water, and air and air-borne particles—known as partitioning—both of which affect uptake into the atmosphere, transport and subsequent deposition.

That endosulfan is actually being transported by air from the fields and glasshouses where it is used and then redeposited, often at very remote locations, is evidenced by the residues found in air, fog, rain, snow and ice described below.

Volatility

Endosulfan is semi-volatile. It evaporates from the soil surface and even more so from plants, particularly during the first week after application. The rate of evaporation increases with temperature, humidity, and wind (Bedos et al 2002). It also evaporates from water: the volatilization half-life from surface waters is greater than 11 days and possibly greater than 1 year (ATSDR 2000).

Laboratory studies *(at 21-22* °C, and 50% relative air humidity):

- 25-30% dissipated from the soil surface to air over 24 hours;
- 64% dissipated from bean leaves; and
- alpha endosulfan is much more volatile than the beta

isomer, and the sulphate is much less volatile, with only 5% released to the air from plants within 24 hours (GFEA-U 2007).

Field studies:

- At maximum temperature of 40 °C, there was 82% loss over 24 hrs, and 89% over 48 hrs, from cotton foliage; and
- at maximum temperature of 29 °C, there was 49% loss over 24 hrs, and 69% over 48 hrs, from cotton foliage (GFEA-U 2007).

In one study in Australia, approximately half of endosulfan applied to soil surfaces dissipated—the alpha isomer in 3-5 days, and the beta isomer in 5-8 days. Even with heavy rainfall for the first few days after application to freshly tilled soil, 34.5% of alpha endosulfan evaporated from the soil within 20 days (GFEA-U 2007). Sutherland et al (2004) claimed 70% of endosulfan volatilises within 2 days.

Kennedy et al (2001), based on studies on endosulfan application in cotton fields in Australia, concluded that 70% of endosulfan is lost from the cotton field through volatilisation, with only 8.5% remaining on the field one month after spraying; 2% is carried away in run-off, 1% remains in the soil, and the remainder is degraded by plants or microorganisms). In other words about 73% of endosulfan applied leaves the site of application and contaminates the wider environment.

Atmospheric half-life

The Stockholm Convention regards a chemical as having the potential for long-range atmospheric transport if its half-life in air is > 2 days. Endosulfan has an atmospheric half-life of 27 days (± 11 days), at 75 °C under experimental conditions. The much lower temperature in the trophosphere would result in a much longer half-life in the air there. Experimental measures have found a half-life for alpha endosulfan of >2.7 days and for beta endosulfan of >15 days. However measurements at Alert, Nunavut in the Canadian Arctic have shown an atmospheric half-life there of 38 years for alpha endosulfan (Hung et al 2002, 2005).

Partitioning

Interchange between air and water, which affects uptake into the atmosphere and redeposition in rain or snow, is described by Henry's Law constant (H)—the higher the value, the higher the deposition.

- Estimates of H for endosulfan vary widely, from 0.71 to 12.9 Pa m^3 mol^{-1} for the alpha isomer at 20^0C (GFEA-U 2007)

Gas-particle partitioning for endosulfan is poorly understood. Values given by GFEA-U (2007) are 0.166 for alpha endosulfan and 0.228 for beta endosulfan adsorbed to particles at 0^0C, falling to 0.018 and 0.024 at 20^0C.

Residues in air[2]

Endosulfan, along with PCPs, is regarded as the most abundant POPs pollutant of the global atmosphere (Pozo et al 2006). It has been found in air from one end of the world to the other: the Global Air Passive Sampling (GAPS) study carried out over just 4 months in 2004-2005 found residues of alpha endosulfan in the air at every one of 41 sites with the exception of Antarctica—from Alert in the Canadian Arctic through Europe, Africa, Asia and Central America, to Chile and Australia in the south (see Table 1 for a sample of these)—including in a number of urban areas (Pozo et al 2006).

Table 1: Residues found in GAPS study

Country	Location	TE (ng/m3)
Argentina	Bahia Blanca	18.704
Canary Island	Telde	1.760
Ghana	Accra	0.952
Bolivia	Potosi	0.510
S Africa	DeAar	0.350
Canada	Whistler	0.129
Turkey	Ismir	0.126
Iceland	Malin Head	0.107
USA	Georgia	0.107
Kuwait	Kuwait City	0.101
Bermuda	Bermuda	0.077
Canada	Alert	0.069
Philippines	Manilla	0.066
Malaysia	Dum Valley	0.066
China	Chengdu	0.047
Australia	Cape Grim	0.027
Source: Pozo et al 2006		

An earlier pilot study carried out over 2002-2004 found much higher levels in Toronto, Canada (0.104 ng/gm) and at Cape Grim, Tasmania in Australia (0.719 ng/gm), probably resulting from Australia's own use of endosulfan. Residues at Whistler Mountain in Canada (0.321 ng/gm) were believed to have come from India (Harner et al 2006).

Residues in air are generally described in terms of the distance over which they have travelled—long-range to remote locations such as the Arctic, and Antarctic; regional distribution including to local mountain ranges; and short range including localised spray drift and ambient or background air concentrations resulting from drift and/or volatilisation.

In most atmospheric studies alpha endosulfan is present in greater amounts than the beta isomer (Tuduri et al 2006), but at an order of magnitude lower than elsewhere in the environment.

Long range

Endosulfan was first noticed in the Artic air in 1986-87, and was measured from early 1993 through to the end of 1997 at concentrations of 0.0042-0.0047 ng/m^3 and has been routinely found there, widely distributed, ever since (GFEA-U 2007). Unlike the other POPs, concentrations have not decreased with time—due to ongoing use they

2 Unless otherwise specified, the values given are for total endosulfan i.e. alpha + beta + the sulphate. AE = alpha endosulfan; BE = beta endosulfan, ES = endosulfan sulphate

are actually increasing (NCP 2003)—and are exceeded only by HCH and HCB (Hung et al 2002). It has been found at many sites across the Canadian Arctic, in 90% of air samples at Amerma in the Russian Arctic (GFEA-U 2007), and recently in the European Arctic at Bjørnøya (Bear island) (Kallenborn et al 2007).

Modelling data has also shown that endosulfan released in Central Europe may spread over the Northern Atlantic as far as Greenland (GFEA-U 2007).

Regional transport

Endosulfan has been described as one of the most abundant and ubiquitous air contaminants in continental North America (GFEA-U 2007). Air sampling at 40 stations (31 in Canada, 5 in USA and 4 in Mexico, Belize and Costa Rica) found alpha endosulfan at 39 of the stations and beta at 30 (Shen et al 2005).

In Canada endosulfan has been measured in the air in both agricultural areas and in so-called receptor sites demonstrating regional atmospheric transport, including in the Great Lakes Basin, the City of Toronto, the Fraser Valley in British Columbia, Prince Edward Island, Quebec, Ontario and Saskatchewan. 100% of air samples collected at 5 sites across Canada in the summer of 2003 contained endosulfan, at high levels of 5.71 ng/m^3 (AE) (Yao et al 2006).

Alpha endosulfan was present in 100% of air samples taken on the campus of the University of Maryland beside the Choptank River, Chesapeake Bay over a 7-month period Apr-Nov, with a maximum concentration of 0.68 ng/m^3. The endosulfan was thought to come from sources outside the Choptank River watershed area (Kuang et al 2003). Endosulfan has also been measured in the atmosphere in a number of sites from northern Michigan to southern Louisiana (Hoh & Hites 2004).

Regional transport of endosulfan has been identified in China and over the Yellow Sea. The beta isomer was found, at levels up to 0.025 ng/m^3, in all 9 day and night-time samples taken at the Ocean University of China, which is in an urban setting in Qingdao on the Yellow Sea coast (Lammel et al 2007). Very high concentrations of endosulfan have also been reported in Guangzhou and Hong Kong and are thought to originate in agricultural areas of East China where it is used in cotton fields, and to have been carried from there by the winter monsoon. Levels at a suburban site in Guangzhou were as high as 2.5 ng/m^3 (AE) and in urban Hong Kong 0.84 ng/m^3 (AE) (Li et al 2007). The air around Lake Taihu contained residues of alpha endosulfan up to 0.888 ng/m^3 (AE) (Qiu et al 2004), with an estimated deposition rate of 25 ng/m^2/day in summer (Qiu et al 2008) indicating that it is rapidly moving out of the air and into the Lake. Other studies have found lower levels of alpha endosulfan in urban Hong Kong and on top of the island's highest point (Louie & Sin 2003).

In Chile alpha endosulfan was found in a concentration gradient that decreased from 0.099 ng/m^3 (AE) in the north to 0.035 ng/m^3 (AE) in the south (Pozo et al 2004).

Mountains

Endosulfan has been found in the air around a number of mountains. Temperate mountains in particular experience effective upslope air movement which brings with it residues originating from regional applications, with residue levels increasing with elevation (Daly et al 2007b).

It has been found as a ubiquitous air contaminant in the mountains of the Canadian Rockies, the California Sierra Nevada (Daly et al 2007a), and the USA's western national parks (Landers et al 2008).

It has also been found in air in the European Central Pyrenees (0.006 ng/m^3 AE) and the High Tatras (0.042 ng/m^3 AE) (van Drooge et al 2004), and in concentrations higher than any other POP in the air in the Mt Everest region (Li et al 2006b).

More recently endosulfan has also been found in the air (and soil) in neotropical montane forests in Costa Rica, by Daly et al (2007b), as a result of regional transport. They found endosulfan to be ubiquitous in the air across the country with very high concentrations at some lowland sites (e.g. 2.3 ng/m^3), and lesser concentrations in the mountain air. However the reverse was true for residues in the soil with higher residue levels (e.g. 3,175 ng/kg) in the mountain soils. The authors explained a process whereby endosulfan used in lowland agriculture is carried by easterly winds to the downwind mountains; forced atmospheric uplift causes the formation of orographic clouds and subsequent rainfall. The drop in temperature with elevation greatly increases the scavenging by the rain of endosulfan from the air (only slightly scavenged at the higher temperatures in the lowlands), leading to greater deposition in rainfall and a build up of residues in the soil because of lower evaporation. The authors suggested that the high soil residues in the mountain forest may be a factor in the observed decline in amphibia in the mountains.

Short-range drift and ambient air contamination

Localised air contamination also occurs, as a result of short-range spray drift and/or volatilisation, exposing people and the environment to unacceptable levels of endosulfan in both rural and urban areas.

Endosulfan was the most prevalent organochlorine pesticide in rural air in South Korea (Yeo et al 2003), and in urban Seoul (Yeo et al 2004). It was also present in air samples taken in Izmir, Turkey (Sofuoglu et al 2004).

In France, endosulfan was found in 79% of indoor air samples in the Paris area (Bouvier et al 2006), and in 100% of air samples taken in urban Strasbourg during July (Scheyer et al 2005).

Endosulfan was found in 66 out of 75 rural air samples taken in California, on the roofs of community buildings such as schools in both rural and urban communities. The mean concentration in urban areas was 3.8 ng/m^3, and in rural areas was 180 ng/m^3 (Lee et al 2002).

It has been found in the air in Belize (GEF CAC 2002), and India (GEF IO 2002).

Ambient air concentrations of endosulfan were found in both farming and non-farming areas of Prince Edward Island in Canada, where it is used in potato cultivation (White et al 2006).

In air-monitoring studies facilitated by scientists from PAN North America, using their 'Drift Catcher' equipment, endosulfan was found in every sample collected at a Florida elementary school surrounded by fields of cabbage. The maximum level of endosulfan found (626 ng/m^3) was 1.8 times the 24- hour acute and subchronic 1-year child Reference Exposure Level (REL) of 340 ng/m3 for endosulfan calculated from the US EPA's inhalation NOAEL. All samples contained alpha endosulfan, and 88% contained beta endosulfan. 38% were above the 24-hour acute and subchronic 1-year-old child REL (PANNA 2007). Repeat sampling between 1 October and 6 December 2007, found detectable levels of endosulfan in 87% of samples. Nine samples (23%) were above the child REL of 340 ng/m3. The highest concentration of total endosulfan observed for a 24-hour period was 1376 ng/m3 (mainly composed of the alpha isomer) and this was 4 times the 24-hour acute 1-year-old REL and 2.8 times the 7-year-old REL (PANNA 2008).

Atmospheric Deposition

Snow

Endosulfan, like other POPs has a marked tendency to deposit out of the air (cold condensation) in remote environments at high latitudes and at high elevations. This is caused by low temperatures and efficient scavenging from the atmosphere, by snow, of both particle-bound and gas-phase pesticides (Hageman et al 2006; Daly et al 2007b).

Alpha endosulfan was first identified in snow in the Canadian Artic in 1986 (Ellesmere Island) and concentrations measured through to 1989 ranged up to 1.34 ng/m^3 (Tuduri et al 2006; GFEA-U 2007).

In 2002-03 endosulfan residues were amongst the most frequently detected in snowpack in seven national parks in arctic, sub-arctic and alpine regions of the US. The highest concentration was 1500 ng/m^3 at Sequoia National Park, the majority of which was regarded as resulting from regional transport. Residues in the Arctic region (peaking at 170 ng/m^3) were regarded as the result of long-range transport (Hageman et al 2006).

Alpha and beta endosulfan were again consistently detected in snowpack near Lake Superior in 1999/2000, at concentrations ranging up to 0.181 ng/l AE plus 0.035 ng/l BE (Burniston et al 2007).

It was one of the most frequently detected pesticides in snow in the Rocky Mountain and Glacier National Parks in the Western US, found at levels up to 2.5 ng/l (AE) (Mast et al 2007).

Alpha endosulfan was found in 100% of samples of snow taken from the Punta Indren glacier in the Italian Alps at concentrations ranging from 0.05 to 0.168 ng/l (Hebert et al 2004).

It appears that very little monitoring has been carried out in Antarctica. However endosulfan sulphate has been found in an ice core sample from the Antarctic region at a concentration of 300 ng/l (Deger et al 2003).

Rainfall

Endosulfan has been found at high levels in rain in various parts of the world, especially in countries still using the pesticide.

In six years of monitoring of rainfall at Lakes Superior, Erie and Ontario, endosulfan was found in 95% of samples, with concentrations of the beta isomer always higher than the alpha isomer. For 20 years, between 1980 and 2000 endosulfan was monitored in rainfall in Prince Edward Island, Nova Scotia, New Brunswick and Newfoundland: the alpha isomer was found in 5.3% of samples and the beta isomer in 11.5% (Tuduri et al 2006; Brun et al 2008). Samples taken at seven US and Canadian sites around the Great Lakes between 1997 and 2003 showed residues of endosulfan peaked in summer corresponding to maximum usage in nearby agricultural areas (Sun et al 2006). Carlson et al (2004) reported mean concentrations of endosulfan as 1.18 ng/l in the rain at five sites round the Great Lakes (US).

Between 1996 and 1998 endosulfan was found in rainfall samples collected at remote high mountain lakes in the Pyrenees, Alps and Caledonian mountains of Europe (Carrera et al 2002).

Endosulfan has also been measured in rainfall in urban areas: between 2000 and 2003, endosulfan was measured in rain in the urban areas of Cuiaba, Brazil at 107 ng/l (Laabs et al 2002), and in Chicago and Jersey City, USA (Sun et al 2006). In 2000, the beta isomer was found in 28%, and alpha isomer in 13%, of rainfall samples, taken on the campus of the University of Maryland beside the Choptank River, Chesapeake Bay over a 7-month period Apr-Nov, with a maximum concentration of 81 ng/l (beta) (Kuang et al 2003).

Endosulfan was found in 85% of rainwater samples taken in urban Strasbourg and rural Erstein in France, in 2002-03, the highest concentration being 3667 ng/l (AE + BE) in Strasbourg; and is also reported for Flanders in Belgium (Scheyer et al 2007).

Between 1997 and 2000 endosulfan and its metabolite was the pesticide most frequently detected in weekly rainfall sampling in Flanders, Belgium (Quaghebeur et al 2004).

Endosulfan was found in 100% of samples of rainwater collected in Hisar, India in 2002, total endosulfan at levels up to 3,020 ng/l (Kumari et al 2007).

Endosulfan was also been found in rainwater in Malawi (GEF SSA 2002).

Dust

Deposition of endosulfan in dust is also of concern. Monitoring in the Caribbean, at the Virgin Islands and Trinidad, has identified endosulfan at all sites, blown there in dust from Mali in the African Sahara/Sahel region (Garrison et al 2006).

Climate change and deposition

Endosulfan is more easily deposited onto water than it is onto ice, and it is expected that as the ice in the Arctic—presumably also Antarctic—diminishes with increasing global temperatures, the deposition of endosulfan in polar waters will increase and hence become more available to plants and animals in the marine food-web (NCP 2003).

Environmental Contamination

Endosulfan residues can be found throughout the world, throughout the environment. In remote regions such as the Arctic, this results from long-range atmospheric transport; in other regions it is from local use. Residues in air, rainfall, and snow are covered in the preceeding section on transport and deposition.

Soil Contamination

Very high levels of contamination have been found in Ethiopia, with total endosulfan reaching levels of 56,000 *u*g/kg in the soil of a state farm where organochlorine insecticides have been used for about three decades. The Upper Awash Agro Industry Enterprises grows cotton, fruits, vegetables, allium flowers and cereals, and their annual endosulfan use is 29,000 litres, estimated to be about 10 tonnes active ingredient (Westbom et al 2008).

In Australian cotton fields where endosulfan is applied 3 times throughout the cotton-growing season, residues from the previous season's spraying were found in the soil at the beginning of the next season (at 10 to 80 *u*g/kg), indicating a continual build up in the soil (Kennedy et al 2001).

Similarly, in Tamil Nadu, India, 100 to 1,000 *u*g/kg residual endosulfan sulphate was found at the beginning of the rice season, with this level increasing to 22,000 *u*g/kg during the season-–still present at 5,500 *u*g/kg at 210 days after application (Jayashree & Vasudevan 2007b), again indicating accumulating residual levels.

Although at much lower levels, endosulfan contamination of the soil in cotton fields of the Punjab has been shown to increase with time, by a factor of 5 over the course of 3 years: in 1995 the residue after application was 7.3 *u*g/kg reducing to 2.4 *u*g/kg after 22 days. But in 1998 in the same field the levels were 35.6 *u*g/kg reducing to 22 *u*g/kg after 22 days, despite the insecticide being applied at the same rate (Vig et al 2008).

All samples of soil taken in cotton-wheat, paddy-wheat and sugarcane fields in Haryana, India, were contaminated with endosulfan at levels ranging up to 39 *u*g/kg (Kumari et al 2008).

It has also been found in the soils of in the northern Indo-Gangetic plains (Singh et al 2007); Hong Kong (Zhang et al 2006), and the Taihu Lake Region of China (Wang et al 2007b); Ghana (Ntow 2001), Senegal and Kenya (Westbom et al 2008), Portugal (Gonçalves & Alpendurada 2004), Czech Republic (Shegunova et al 2007), rice fields in Spain (Gamon et al 2003), Colombia (at 350 *u*g/kg), Honduras, Nicaragua, and Panama (GEF CAC 2002), and in the soils of environmental reserves in Brazil (Rissato et al 2006).

Surface waters and sediment contamination

Published reports of endosulfan contamination of surface water between 1982 and 2003 contain 606 detections in Canada, USA, Sweden, Australia, South Africa, and Argentina (Schulz 2004), a far from complete record with many more reports since then. The US EPA (2007c) reported 667 detections between 1980 and 1999 for beta endosulfan in the USA alone.

The contamination of surface waters has frequently occurred at levels above those reported to cause adverse effects on aquatic life (Schulz 2004). The US EPA (2007c) reports toxicity to estuarine/marine amphipods of endosulfan in sediment at concentrations as low as 1.5 *u*g/kg of pore water (water filling spaces between grains of sediment). Other estimations for hazardous concentrations for aquatic organisms include 0.2-11 *u*g/l for fish (Kennedy et al 2001); and a mean level of 0.02 *u*g/l for effects on 5% of aquatic organisms (Bollmohr et al 2007). All of the figures reported below exceed this level.

Endosulfan reaches surface waters as a result of direct deposition and runoff from agricultural use. Reports of endosulfan concentrations in run-off include 100 *u*g/l in southern USA, 45 *u*g/l in Australia, 66.5 *u*g/l in India (Menone et al 2008), 12,082 *u*g/kg of suspended particles in South Africa (Schulz 2001), and up to 1,530 *u*g/l in ditch water during application on adjacent fields in British Columbia, Canada (Schulz 2004).

Kennedy et al (2001) found "significant contamination of all runoff water throughout the entire cotton-growing season in New South Wales", Australia, with residue levels in the runoff reaching 10 *u*g/l seven days after aerial application, and typically being 2-10 *u*g/l. Major storms soon after application can cause runoff of 10% of the endosulfan applied.

Concentrations of endosulfan in Australian rivers during the cotton growing season were reported to be in the range of 0.02 to 0.2 *u*g/l, significantly exceeding the 0.01 *u*g/l guideline for ecosystem protection set by the Australia and New Zealand Conservation Council in 1992—due to nearly continuous low level input from spray drift and vapour transport representing "a steady drizzle", and occasional higher input from run-off (Raupach et al 2001).

Endosulfan has been found in 47% of surface water samples tested in an agricultural region of Western Cape, South Africa. 37% of the detections exceeded the EU's

limit of 0.1 *u*g/l, and reached levels of 3.6 *u*g/l. The main source was reported to be washout from the agricultural soils after irrigation and rainfall (Dalvie et al 2003). A pervious study in Western Cape, reported by Dalvie et al (2003), found endosulfan in 26 out of 27 Elgin dams at levels up to 626 *u*g/l; Bollmohr et al (2007) report 12.7 *u*g/l particle-associated endosulfan.

Levels of 1.85 *u*g/l of endosulfan were found in water samples from the Selangor River in Malaysia in 2003 (Leong et al 2007). It has also been found in water and sediment in rivers in Perak, Juru, Perai, Muda and Bernam (GEF SEA SP 2002).

Other findings of surface water contamination:

- India—in a number of rivers (Selvakumar et al 2005), including water from the Yamuna River at Delhi, India (Aleem & Malik 2005); streams, ponds and canals of the northern Indo-Gangetic alluvial plains (Singh et al 2007); water of the Gomti River, a tributary of the Ganges, at 0.09 *u*g/l (ES) (Malik et al 2008); water and sediment in prawn ponds (Amaraneni 2006); and levels of 2.4 *u*g/l in Kolleru Lake and 2.0 *u*g/l in Vellar River believed to be caused by a nearby endosulfan manufacturing facility (Sarkar et al 2008);
- China—sediment of Lake Taihu at 50.5 *u*g/kg (ES) (Huang et al 2006); sediment of the Tonghui River (Zhang et al 2004); and water and sediment in the Minjiang River estuary 0.215 *u*g/l (BE) (Zhang et al 2003);
- sediment in the Wu-Shi River estuary, Taiwan, at 10.5 *u*g/l (ES) (Doong et al 2002);
- water and sediment of Uluabat Lake, Turkey (Barlas et al 2006);
- water and sediment in Ghana (Ntow 2001; Ntow et al 2008); lakes in Malawi (GEF SSA 2002); and in all samples of water and sediment from the Kafue River, Zambia (Syakalima et al 2006);
- In Benin, following its reintroduction into cotton growing in 1998-1999, endosulfan was found in almost all water samples taken in the W region transboundary biosphere reserve (which covers over one million hectares in Benin and Burkina Faso), and in Pendjari Reserve, at levels up to 0.46 *u*g/litre (Glin et al 2006);
- sediment in Lake Kinneret, Israel at 276 *u*g/kg (GEF M 2002);
- a number of rivers in the USA (Hinck et al 2008); the National Sediment Quality Survey found endosulfan stream sediments in 30 out of 76 watersheds it tested for residues (US EPA 2002); year-round detections of endosulfan in freshwater canals draining from agricultural areas in South Florida into the Everglades and Florida Bay, indicating chronic exposure to aquatic species (DeLorenzo et al 2002); 0.45 *u*g/kg (ES) in Florida surface waters and 120 *u*g/kg (ES) in sediment (Pfeuffer & Rand 2004); 571 *u*g/kg in the sediment of tailwater ponds collecting runoff from lettuce fields in California and 17.7 *u*g/kg in a nearby creek (Weston et al 2004); frequent detections in the water of 30 lakes in Canada and the northeastern USA (Muir et al 2004); in the sediment of mountain lakes in the Rocky Mountain and Glacier National Parks in Western USA at up to 1.2 *u*g/kg (ES) (Mast et al 2007), with endosulfan sulphate steadily increasing in the sediment of the Rocky Mountains lakes since 1954, reaching a maximum in 2003 (Usenko et al 2007);
- Argentina—in agricultural runoff, stream water, and river bottom sediments (Jergentz et al 2004, 2005; Menone et al 2008); endosulfan sulphate was the most frequent and abundant contaminant found in sediment of two creeks in south-eastern Argentina which contribute to coastal pollution (Miglioranza et al 2004a);
- sediment from a coastal wetland in Mexico at 0.814 *u*g/kg (AE) (Hernandez-Romero et al 2004); river water in Brazil (GEF SA 2002); and surface waters in Guatemala, Jamaica, Honduras and Colombia (GEF CAC 2002);
- suspended particles in small streams in Brittany, France (Schafer et al 2007); water from rivers in Portugal (Cerejeira et al 2003), and Greece (Golfinopoulos et al 2003; Konstantinou et al 2006); water from the remote European mountain lakes in the Alps, Pyrenees and Caledonian mountains (Vilanova et al 2001); and
- Azerbaijan—sediment from a wetland adjacent to a wastewater treatment plant contained 31 *u*g/kg (BE) (Swartz et al 2003).

Groundwater contamination

There are many reports of groundwater contamination in India:

- Haryana - all samples of water from tube wells in agricultural areas were contaminated with endosulfan, with 83% of samples exceeding the EU maximum permissible level of 0.1 *u*g/l, with levels up to 0.405 *u*g/l (Kumari et al 2008);
- Hyderabad City - all the samples of domestic well water contained endosulfan, at levels up to 11.23 *u*g/l, assumed to derive from agriculture near the city (Shukla et al 2006); and
- Thiruvallur area of Tamil Nadu where endosulfan is used on rice - total endosulfan in open well and bore wells ranged from 1.1 to 19.2 *u*g/l (Jayashree & Vasudevan 2007a).

It has also been found in 8% of samples from rural wells in 4 areas of Punjab, Pakistan (Tariq et al 2004).

The US reported endosulfan in 1.3% of wells tested and endosulfan sulphate in 0.3%, prior to 1990 (US EPA 2002).

Endosulfan has recently been found in 38% of groundwater samples in Portugal, with 12% of them exceeding the European Union's limit of 0.1 *u*g/l (Goncalves et al 2007).

In South Africa Dalvie et al (2003) found endosulfan in 32% of groundwater samples taken in farming areas in the Western Cape at levels up to 0.89 *u*g/l.

It has been found in the groundwater in Morocco (El Bakouri 2007) and Guatemala (GEF CAC 2002).

Marine sediments and seawater

Endosulfan and its metabolite have also been found in marine waters and sediment although generally at lower levels than those in freshwater. Only those figures exceeding the Bollmohr et al (2007) hazard level of 0.02 *u*g/l are given below:

- endosulfan contamination of Arctic seawater has been observed since early 1993 (Jantunen & Bidleman 1998; Weber 2006; GFEA-U 2007) and is now so widespread in the surface water that it has been described as ubiquitous (Bidleman et al 2003);
- inland coastal waters of Malaysia (0.4 *u*g/l) and Philippines, and sediment in the Straits of Malacca (GEF SEA SP 2002). It has been found in marine water and sediment around India (GEF IO 2002); concentrations of endosulfan sulphate reached 0.4 *u*g/l in sediment taken from the mouth of the Hugli estuary in the vicinity of the Sundarban mangrove environment in eastern India (Bhattacharya et al 2003);
- endosulfan sulphate was found at 0.025 *u*g/l in sediment on the Black Sea coast of Turkey in 2001-2003, and at low levels in seawater there (Ozkoc et al 2007); in the sediment of Alexandria Harbour, Egypt (Barakat et al 2002); and in a coastal lagoon in Spain (GEF M 2002);
- in the water of harbours in South Africa (Fatoki & Awofolu 2004); and
- in the coastal waters of Honduras and Jamaica, the sediment of Kingston Harbour (GEF CAC 2002); and in coastal lagoons of the subtropical Mexican Pacific (GEF M 2002).

Biota contamination and poisonings

Poisoning of non-target biota is widespread. In Thailand, where endosulfan was used for the control of golden apple snails in paddy fields, a survey in five provinces revealed that almost all farmers in every province reported deaths of fish, snakes, frogs, eels and toads (UNEP/FAO 2006a).

Polar regions

Contamination of the Arctic marine mammals with POPs was first discovered in the 1960s (Li & Macdonald 2005), and since then endosulfan has been consistently measured in Arctic wildlife.

Vorkamp et al (2004) found residues in every species they tested in Greenland:

- in terrestrial species—ptarmigan, lamb, caribou, muskox;
- freshwater fish—Arctic char;
- marine fish (up to 50 *u*g/kg)—cod, redfish, salmon, halibut, wolfish, capelin, sculpin;
- marine invertebrates—shrimp, crab, scallop;
- seabirds—common eider, king eider, kittiwake (up to 62 *u*g/kg), thick-billed murre; and
- marine mammals—ring seal, harp seal, minke whale, narwhal (up to 64 *u*g/kg).

The highest levels were found in narwhals and the kittiwake, with high levels also in marine fish and crab.

Other residues of endosulfan found in the Arctic include:

- in lichen (Kelly et al 2007);
- in adipose tissue and blood of polar bears from Svalbard (GFEA-U 2007);
- in the blubber of belugas at 15 sites in the Canadian arctic between 1993 and 2001, at levels reaching 94 *u*g/kg (Stern et al 2005); and
- in the liver of northern fulmar (GFEA-U 2007).

Contamination is also occurring in Antarctica: both alpha endosulfan and endosulfan sulphate have been found in blubber of elephant seals in Antarctica with significantly higher relative proportions in pups compared with adults, probably due to maternal transfer (Miranda-Filho et al 2007). The levels found (median 3.2 and 2.68 *u*g/kg lipid for adult males and females) are similar to those found in Greenland.

Aquatic Species

For residues in fish and other seafood, see under Exposure – Food. Residues have also been found in:

- African catfish, crab, toad, and frogs in the rivers of Dridji, Benin at levels up to 75 *u*g/kg (Glin et al 2006);
- mussels on the Black Sea coast of Turkey (Ozkoc et al 2007);
- marine zooplankton, oysters, clams and fish around India (Sarkar et al 2008);
- 86% of tadpoles sampled in some locations in California (Sparling et al 2001);
- crocodiles in Belize (Wu et al 2000, 2006); and
- anuran amphibians in Argentina (Jofre et al 2008).

Additionally there have been a number of fish kills attributed to endosulfan. A mass fish kill occurred in Sudan in 1988, when empty endosulfan drums were washed in an irrigation canal; and the same practice also caused fish kills in Senegal in 1998-99 (Glin et al 2006). In 1995 aerial spraying of endosulfan on tomato fields in Dagan in the Senegal River valley caused fish to die along several kilometres of the river (Glin et al 2006).

A huge fish kill in Alabama, of an estimated 240,000 fish along a 16 mile stretch of the Big Nance Creek, was believed to be caused by endosulfan when concentrations in the water were found to be two times higher than those known to kill fish (PANNA 1996).

Fish kills in estuarine waters in South Carolina were believed to be caused by endosulfan concentrations reaching 1.44 *u*g/l (Schulz 2004); and fish kills in Jamaica resulted from use of endosulfan on coffee (GEF CAC 2002).

Terrestrial species

In Zimbabwe aerial spraying of endosulfan against tsetse flies resulted in the contamination of non-target birds, reptiles, amphibians, fish, and some mammals in the Zambezi River valley (Glin et al 2006).

In South Africa 370 incidents of wildlife poisoning were reported between 1980 and 1995 (GEF SSA 2002).

Benin: *Farmers using Callisulfan as a cotton pesticide also reported dramatic effects on the environment at*

large. One farmer in the Borgou province stated that "Earthworms emerged from the soil, and subsequently died. Then, birds came to eat the earthworms and they died as well." A farmer in the Aklampa area reported: "This year the product is very effective. It kills everything—even snakes". Another farmer reported that "…fields smelt awful two or three days after spraying because virtually every living thing had been killed and started rotting". In Goumori, lots of fish were reported to have died from pesticides running off cotton fields (Ton et al 2000).

In New Zealand, symptoms ranging from weight loss to death have been reported in baby herons, and seizures in a dog (ERMANZ 2007b).

Other examples of biota contamination:

- 86% of frogs tested in California had residues of endosulfan (Sparling et al 2001);
- vultures in South Africa (van Wyk et al 2001);
- in 92% of samples from three bird species in Argentina, with levels up to 4,276 *u*g/kg fat (Cid et al 2007);
- in the eggs of all water bird species tested at Tai Lake in China; 78% of little egret eggs contained residues up to 134.7 *u*g/kg (AE + BE) (Dong et al 2004);
- in birds at up to 66 *u*g/kg (BE), and at lower levels in amphibians, in a tropical conservation area in northwest Costa Rica (Klemens et al 2003);
- in the blood of booted eagles in Spain at levels up to 239 ug/l AE, 90 ug/l BE and 216 ug/l ES (Martinez-Lopez et al 2008);
- in marsh antelope in Zambia (Sichilongo & Torto 2006); and
- in wild rats in Zimbabwe (Kuvarega & Taru 2007).

Non-target Plants

Endosulfan has been found in:

- grasses in the Mt. Qomolangma (Everest) region of the Tibetan Plateau (Wang et al 2007a);
- 95% of samples of Himalayan spruce needles from the Central Himalayan region (Zhangmu-Nyalam), with levels increasing with latitude (Wang et al 2006b);
- spruce and pine needles in the mountains of western Canada (Davidson et al 2003);
- in the bark of trees from every one of the 32 countries sampled from all over the world between 1992 and 1995, including India (1500 *u*g/gm), South Korea (1100 *u*g/gm), Philippines (540 *u*g/gm), Japan (450 *u*g/gm), Iran (310 *u*g/gm), Australia (110 *u*g/gm), New Zealand (32 *u*g/gm) and China (14 *u*g/gm), as well is in Africa, North and South America and Europe (figures are averages for the country for endosulfan sulphate) (Simonich & Hites 1995, 1997);
- lichen in the Canadian Rockies (Daly et al 2007a);
- moss in Singapore at 6.52 *u*g/kg (Lim et al 2005);
- bulrushes in an Argentinean lake (Miglioranza et al 2004b); and
- aquatic plants in Nigeria (GEF SSA 2002).

Insecticide resistance

Resistance to endosulfan has developed in at least 28 species affecting at least 22 crops. The insects that have developed resistance include aphids, whitefly, mosquito, cotton bollworm, tobacco budworm, coffee berry borer, Colorado potato beetle, leafhoppers, midges, diamond-back moth, cutworms, and thrips. The crops include cotton, tobacco, coffee, cocoa, grape, grains, fruit such as pears, berry fruit, hazelnuts, sugarcane, and many vegetables (Whalon et al 2008). Resistance has not been reported yet on soy or tea.

Alternatives to Endosulfan

Clearly effective alternatives exist as so many countries have banned all use of endosulfan. Manuweera et al (2008) studied the productivity of crops in Sri Lanka following the banning of a number of insecticides, including endosulfan, that were being used for self-poisoning. They found no drop in yields in paddy rice, cereals, pulses, tea, rubber, coconut or the vegetable crops they studied, other than normal annual fluctuations, and no increase in the cost of paddy production or the production of any other crop they studied.

Alternative insecticides

There are many other synthetic chemical insecticides on the market, but most of these also have a range of adverse health and environmental effects, such as endocrine disruption, cancer, neurological damage, groundwater contamination, persistence, etc. Hence, their use is not recommended to replace endosulfan.

There are some insecticides derived from natural plant extracts that can kill or repel insects; some deter insects feeding, or inhibit their growth. Natural soaps and minerals can also be used, as can naturally occurring pathogens like *Bacillus thuringiensis* (Bt) used as a spray—NOT as a genetically engineered part of the crop itself.

Care must be taken even with natural plant extracts as some, such as pyrethrum, can have toxic effects on beneficial insects, animals, and humans. Other plant extracts that can be used to replace endosulfan include neem, lemon grass, garlic, ginger, marigold, quassia, turmeric, and many more. For a description of 35 plant extracts that can be used, including the pest they will control and how to make the plant extract spray, refer to PAN Germany's 2008 publication *How to Grow Crops without Endosulfan*. Pests covered include those of rice, cotton, coffee, corn, fruit, and vegetables.

Generally an insecticide, even a natural one, should be regarded as the choice of last resort, with the primary focus being placed on alternative pest management practices that prevent the need for a spray.

Alternative or ecological pest management

Alternative or ecological pest management focuses on sustainable ecological solutions that prevent pest build up. It takes a holistic approach to crop management that recognises pests as an integral part of the whole agroecosystem, forming a complex with beneficial insects, weeds, diseases and crops. The self-regulatory

mechanisms of a highly biodiverse farming system help keep pest species in balance.

Elements of alternative or ecological pest management:

- designing a farm ecosystem that encourages biodiversity, providing habitats for beneficial insects;
- using resistant, often indigenous, crop varieties;
- diversifying crops by intercropping, rotation, and use of multiple varieties;
- cultural practices that encourage healthy soils and hence healthy plants, such as fallowing, appropriate tillage, water management, mulching, and use of animal manures, green manures, vermicasts, composts, liquid bio-fertilisers, and enhanced indigenous micro-organisms;
- cultural practices that contribute to the suppression of pest populations such as varying times of sowing, planting and harvesting, adjusting row width, use of trap crops, and appropriate pruning;
- companion planting to deter pests;
- accurate identification of both pests and beneficial insects and knowledge of their life cycles, habitats, and periods of population expansion and vulnerability;
- enhancing the habitats and hence populations of (or introducing) natural enemies such as parasitoids like the *Encarsia* wasp and predators like the damselfly and spiders, as well as birds and snakes where appropriate; other beneficial insects that control pest for which endosulfan is used include Braconid, *Cotesia* wasp, damsel bug, *Diadegma* wasp, carabid beetle, hoverfly, lacewing, ladybird beetles, Minute pirate bug, praying mantis, predatory mite, rove beetles, spiders, tachinid fly, *Tiphia* wasp, and *Trichogramma*—details of which pests are controlled by each insect can be found in PAN Germany (2008);
- field sanitation—removing infested plant material including crop residues to reduce carryover of pests from one planting to the next;
- systematic scouting of crops for pests and natural enemies, either regularly or at susceptible times, sometimes involving the use of sweep nets, sticky traps, and pheromone traps;
- use of mechanical methods such as light traps, fruit fly traps, trenches (e.g. to prevent migration of rice molluscs into paddy fields), nets, reflective ribbon, bird perches, pheromone traps, sticky board traps, soil baits, soil traps, bagging of fruit, and plant ash; and
- use of pheromone traps to trap insects and pheromone dispensers to disrupt mating

(SIBAT 1999a, 1999b; OISAT 2004; PAN Germany 2008).

The Online Information Service for Pesticide Management in the Tropics (OISAT), established by PAN Germany, and PAN Germany's (2008) publication contain extensive information on managing particular pests in specific crops without the use of endosulfan.

The management of earthworms in sports fields, golf putting greens, and between airport runways can be achieved without endosulfan by simply creating conditions that discourage the presence of the worms. Increasing the acidity of the soil by the use of acidifying fertilisers such as ammonium sulphate, ammonium nitrate, or iron sulphate all decrease earthworm activity (Kirby & Baker 1995).

Organic cotton

Successful organic cotton growing is already occurring in Benin, Mali and Senegal, as a result of NGO pilot projects based on the IPM Farmer Field School approach. Techniques employed by these include training to recognise pests and their natural enemies, collection and destruction of pests, recognition of diseases, how to evaluate the level of pest damage that requires intervention, and preparation and use of neem (Glin et al 2006). In Benin, the area under organic cotton grew from 500 hectares in 2005 to an estimated 1,800 hectares in 2008 (PAN UK 2008).

Farmers then use a range of non-chemical strategies for pest control based on encouraging natural predators, and on cultural practices such as selection of resistant varieties, planting early maturing varieties which reduce risk of pest attacks, use of rotation and trap crops (Glin et al 2006).

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(Endnotes)

1. Sources include Extoxnet http://extoxnet.orst.edu/pips/endosulf.htm; Chemical Database (Environmental Chemistry.com; http://environmentalchemistry.com/yogi/chemicals/cn/Endosulfan.html; PAN Pesticides Database http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC35085; Chemical Industry.com http://www.chemindustry.com/chemicals/547090.html; ACVM database of currently registered Veterinary Medicines, Plant Compounds and Vertebrate Toxic Agents http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm; IPCS. 2000. Endosulfan (Poison Information Monograph 576). http://www.inchem.org/documents/pims/chemical/pim576.htm; El Hindi et al (2006); Glin et al (2006).
2. Sources include: Hindustan Insecticides Ltd http://www.hil-india.com/products.htm; Makhteshim-Agan Industries, http://www.ma-industries.com; GFEA-U 2007.
3. Philippines has banned the 35per cent formulation of endosulfan and permitted a 5per cent formulation only. However no such formulations are available or used in the Philippines, so the restriction is regarded as a de facto ban. Also, there were exemptions provided to agri-food corporations Dole and Del Monte, which was only to apply over a phase out period of 2 years but continued indefinitely.
4. Sources include: GEF (2002); ERMA (2006);
UNEP/FAO. 2001. PIC Circular XIII. June. http://www.pic.int/home.php?type=t&id=50;
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5. Sources include: ERMA (2006); GEF (2002); UNEP/FAO (2006a).

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Pesticide Action Network Asia and the Pacific (PAN AP) is one of five regional centres of PAN, a global network working to eliminate the human and environmental harm caused by pesticides, and to promote biodiversity-based ecological agriculture.

"Our vision is a society that is truly democratic, equal, just, culturally diverse, and based on food sovereignty, gender justice and environmental sustainability". Thus PAN AP asserts people's food sovereignty based on the right to food for all, founded on the right to land and productive resources and the right of communities to decide on our own food and agriculture policies. We are committed to protect the safety and health of people and the environment from pesticide use, and genetic engineering in food and agriculture. We strive to protect and promote the rights, equality and dignity of women. We will promote and protect biodiversity based ecological agriculture. Our goal is to strengthen people's movements to eliminate hunger and achieve food sovereignty. We endeavour to achieve these goals by empowering people within effective networks at the Asia and the Pacific, and global levels.

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