

Endosulfan Meets the POPs Screening Criteria

Pesticide Action Network (PAN) International Prepared for PAN International by PAN Asia & the Pacific June 30, 2008

Endosulfan, including both isomers, fulfils the screening criteria specified in Annex D of the Stockholm Convention. Sources of scientific information include critical reviews prepared by recognized authorities and peer-reviewed scientific publications.

Evaluation of Endosulfan against the criteria of Annex D

1. Persistence

Annex D screening criteria

- (i) Evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months; or
- (ii) Evidence that the chemical is otherwise sufficiently persistent to justify its consideration within the scope of this Convention;

Evidence

- (i) The half-life in water is reported to be from 1 month to 6 months under anaerobic conditions (ATSDR 2000); the half-life in a water/sediment microcosm in a Brazilian wetland has been measured as more than 2 months (Laabs et al 2007); the half-life in soil of total endosulfan under aerobic conditions has been reported as 44.5 months (US EPA 2007c), and up to 6 years (GFEA-U 2007).
- (ii) Field studies in India and Australia where endosulfan was used on cotton crops have shown that residual levels in the soil at the beginning of the season are higher than they were at the beginning of the previous season indicating a continual build-up in the soil (Kennedy et al 2001; Jayashree & Vasudevan 2007b; Vig et al 2008).

Endosulfan's persistence has resulted in it becoming a ubiquitous global contaminant of soil, sediment, fresh and marine waters, aquatic and terrestrial biota, and human food.

Conclusion: There is sufficient evidence that Endosulfan meets the persistence criterion.

2. Bio-accumulation

Annex D screening criteria

- (i) Evidence that the bio-concentration factor or bio-accumulation factor in aquatic species for the chemical is greater than 5,000 or, in the absence of such data, that the log K_{ow} is greater than 5;
- (ii) Evidence that a chemical presents other reasons for concern, such as high bioaccumulation in other species, high toxicity or ecotoxicity; or
- (iii) Monitoring data in biota indicating that the bio-accumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention;

Evidence

- Although estimates of log K_{OW} are slightly less than 5 (4.65 for alpha and 4.34 for beta endosulfan) (GFEA-U 2007), a bioconcentration factor of >11,000 has been recorded for at least one aquatic species (Jonsson & Toledo 1993).
- (ii) Additionally, endosulfan has an even greater potential to bioaccumulate in terrestrial species than in aquatic species because of its high log K_{OA} (>10 for alpha and beta isomers), with predicted biomagnification factors in wolves of 5.3 at age 1.5 years, 17.9 at 2.25 years and of 39.8 at 13 years (Kelly & Gobas 2003, supporting data). The biomagnification factor for other herbivorous and carnivorous terrestrial species is calculated as ranging from 2.5 to 28 (Kelly et al 2007).
- (ii) Monitoring data have shown increasing concentrations of endosulfan in age-adjusted beluga (Braune et al 2005), and in freshwater char (Evans et al 2005). There is evidence of bioaccumulation in fish in Argentina, with a biomagnification factor greater than that for DDT and most other POPs (Menone et al 2000), and in rats (Kuvarega & Taru 2007). There is evidence of bioconcentration in plants too: in bulrushes with a bioconcentration factor higher than that for DDT (Miglioranza et al 2004b), in grasses (Wang et al 2007a), and in conifer needles—where total endosulfan in two-year old needles was three times higher than those in one-year old needles (Landers et al 2008). There is evidence of bioaccumulation resulting from maternal transfer of endosulfan in elephant seals in Antarctica, where significantly higher relative proportions were found in the pups compared with the adults (Miranda-Filho et al 2007).

Endosulfan residues are also commonly found in human placental tissue, umbilical cord blood and breast milk, and endosulfan is transferred to the foetus and newly-born infant (Cerrillo et al 2005; Fukata et al 2005; Damgaard et al 2006; Torres et al 2006; Shen et al 2007, 2008; Pathak et al 2008). Residues of endosulfan in breast milk in Bhopal, India in 2003 were 8.6 times the average daily intake levels recommended by the World Health Organisation (Sanghi et al 2003). At least some of the residues in humans are believed to have resulted from the consumption of food containing residues of endosulfan (Campoy et al 2001; Sanghi et al 2003; Carreno et al 2007).

Conclusion: There is sufficient evidence that Endosulfan meets the bioaccumulation criterion.

3. Potential for long-range environmental transport

Annex D screening criteria

- *(i)* Measured levels of the chemical in locations distant from the sources of its release that are of potential concern;
- (ii) Monitoring data showing that long-range environmental transport of the chemical, with the potential for transfer to a receiving environment, may have occurred via air, water or migratory species; or
- (iii) Environmental fate properties and/or model results that demonstrate that the chemical has a potential for long-range environmental transport through air, water or migratory species, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For a chemical that migrates significantly through the air, its half-life in air should be greater than two days.

Evidence

- (i) Residues of endosulfan have been found in biota and in environmental media at locations far distant from where it has been released. It has been found in biota and ice in both the Arctic (Vorkamp et al 2004; Kelly et al 2007; Stern et al 2005) and Antarctic (Miranda-Filho et al 2007). It has been found in grasses on Mt Qomolangma (Everest) region of the Tibetan Plateau (Wang et al 2007a) and in spruce needles of the Central Himalayan region (Wang et al 2006b); in lichen in the Canadian Rockies (Daly et al 2007a), and in lichen and conifers in the western national parks of the USA (Landers et al 2008).
- (ii) Endosulfan has been consistently measured in air all over the world, including in remote locations in the Arctic, high mountain areas in Asia (Himalayas), Europe, and North America, as well as tropical mountains in Costa Rica. Levels of endosulfan in the air are frequently amongst the highest of the pollutants measured. The Global Air Passive Sampling study resulted in a geometric mean value of 62 pg/m³ for total endosulfan, well above the next most abundant, PCPs with a mean of 17 pg/m³. In the polar regions endosulfan levels (2.0 pg/m³) were second only to PBDEs (3.7 pg/m³), and well above DDT (0.5 pg/m³), dieldrin (0.14 pg/m³) and the other POPs (Pozo et al 2006).

It has also been consistently measured in precipitation: in snow in the Canadian Arctic (Tuduri et al 2006) and US national parks (Hageman et al 2006; Mast et al 2007), as well as in ice in the Italian Alps (Herbert et al 2004) and Antarctica (Deger et al 2003); and in rain in Asia (Kumari et al 2007), Africa (GEF SSA 2002), Europe (Carrera et al 2002; Quaghebeur et al 2004; Scheyer et al 2007), North America (Kuang et al 2003; Carlson et al 2004; Sun et al 2006; Tuduri et al 2006; Brun et al 2008), and Latin America (Laabs et al 2002). Residues of endosulfan in the Caribbean are believed to have resulted from deposition in dust carried from the African Sahara/Sahel region (Garrison et al 2006).

Levels of endosulfan have continued to increase in the Arctic, in beluga (Braune et al 2005) and in air (NCP 2003) at the same time as the levels of most POPs have declined. Similar increases have been observed in the freshwater fish char; residues were 2.2 times higher in 2002 than they were in 1992 (Evans et al 2005).

(iii) Endosulfan is semi-volatile. It evaporates from the surface of soil and plants after application. Laboratory studies indicate 25-30% dissipates from the soil surface over 24hrs, and 64% from plant leaves (GFEA-U 2007). Field studies in Australia have found 70% of endosulfan is lost from cotton fields through volatilisation (Kennedy et al 2001; Sutherland et al 2004). The atmospheric half-life of endosulfan under experimental conditions is 27 days. Experimental measures have found a half-life of endosulfan of > 2.7 days and for beta endosulfan of > 15 days. Measurements at Alert in the Canadian Arctic have shown an atmospheric half-life there of 38 years for alpha endosulfan (Hung et al 2002, 2005).

Conclusion: There is sufficient evidence that Endosulfan meets the criterion on potential for long-range environmental transport.

4. Adverse effects

Annex D screening criteria

- (i) Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or
- (ii) Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.

Evidence

(i) Endosulfan is one of the main causes of poisoning in humans in many countries (Kishi et al 2002; Oktay et al 2003; Roberts et al 2004; Wesseling et al 2005). Many deaths have resulted from occupational and accidental non-occupational exposure, as well as self-poisoning, in a number of countries in Africa, Asia and Latin America (PANNA 1999; EJF 2002; El Hindi et al 2006; GEF CAC 2002; Venkateswarlu et al 2000; Glin et al 2006; Mingxin 2007). Acute effects have also been reported in New Zealand and USA (ERMANZ 2007b; Associated Press 2007).

Chronic effects reported in humans include birth defects, congenital reproductive disorders, long-term brain damage, recurrent convulsions, epilepsy, autism, delayed sexual maturity, endometriosis, menstrual disorders, early menarche, male breast enlargement, various cancers, congenital intellectual disability, cerebral palsy, psychiatric disturbances, and vision impairment and loss (Aleksandrowicz 1979; Pradhan et al 1997; Quijano 2002; NIOH 2003; Saiyed et al 2003; Roberts et al 2007; Venugopal 2008).

Many deaths in animals—including fish, wildlife, pets, and livestock—have also been reported, as well as congenital deformities, miscarriages, infertility, stunting of growth, and dwindling populations (PANNA 1996; Ton et al 2000; GEF CAC 2002; GEF SSA 2002; Quijano 2002; NIOH 2003; Schulz 2004; Glin et al 2006; ERMANZ 2007b).

(ii) Toxicological data indicate that endosulfan is very toxic to mammals by skin contact, inhalation or ingestion (GFEA-U 2007). It causes a range of acute neurological effects, including convulsions and death (ATSDR 2000). It damages the liver and kidneys and is toxic to the adrenal gland and pancreas (ATSDR 2000). It causes oxidative stress (Omurtag et al 2008). It is toxic to and suppresses the immune system (ATSDR 2000: Kannan et al 2000: Pistl et al 2003: Garo et al 2004: Lafuente et al 2006; Narita et al 2007). It depresses testosterone levels and may cause reproductive toxicity in humans (ATSDR 2000). It interferes with the steady state levels of oestrogen causing proliferation of MCF-7 human breast cancer cells, and its effects on the endocrine system indicate that endosulfan is likely to cause the onset and/or development of mammary tumours (Soto et al 1994, 1995; Bradlow et al 1995; Toniolo et al 1995; Berrino et al 1996; Dorgan et al 1996; Andersen et al 2002; Cossette et al 2002; Rousseau et al 2002; Grunfeld & Bonefeld-Jorgensen 2004; Kojima et al 2004; Bonefeld-Jorgensen et al 2005; Wozniak et al 2005; Je et al 2005; Laville et al 2006; Lemaire et al 2006; Wong & Matsumura 2006; Chatterjee et al 2008). It targets the prefrontal cortex of the brain (Cabaleiro et al 2008), and may be implicated in Parkinson's disease (Wang et al 2006a; Jia & Misra 2007a). It causes adverse behavioural effects (ATSDR 2000). Exposure in utero causes teratogenic effects (Singh et al 2006). Many studies have shown it to be genotoxic and mutagenic in human cells, rodents, hamsters, fruit fly, fish, tadpoles, oysters, bacteria, microalgae and plants (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; Perez et al 2007; Sharma et al 2007a; Wessel et al 2007; Akcha et al 2008; Menone et al 2008). It is also a tumour promoter (Fransson-Steen et al 1992; Dubois et al 1996; Warngard et al 1996; ATSDR 2000). Toxicity is increased with protein-deficient diets, which are a problem in some of the countries in which endosulfan is still used.

Endosulfan is very toxic to aquatic organisms especially juveniles, and its use results in disruption of the aquatic food chain. Concentrations of endosulfan found in rivers greatly exceed the hazardous concentrations that adversely affect 5% of fresh water and marine organisms as identified in Bollmohr et al (2007).

It is also toxic to amphibians, reptiles, snails, aquatic plants, coral reef organisms, birds, bees, earthworms, and beneficial insects and microorganisms, and is incompatible with IPM (Elzen 2001; Bostanian & Akalach 2004; Bastos et al 2006; Schneider et al 2006; Alizadeh et al 2007; Benamú et al 2007).

Conclusion: There is sufficient evidence that Endosulfan meets the criterion on adverse effects.

Additional information can be found in the PAN International Submission to the Stockholm Convention secretariat

References:

Akcha F, Arzul G, Rousseau S, Bardouil M. 2008. Comet assay in phytoplankton as biomarker of genotoxic effects of environmental pollution. *Mar Environ Res* 66(1):59-61.

Alexsandrowicz DR. 1979. Endosulfan poisoning and chronic brain syndrome. Arch Toxicol 43:65-8.

Alizadeh A, Samih MA, Izadi H. 2007. Compatibility of Verticillium lecani (Zimm.) with several pesticides. *Commun Agric Appl Biol Sci* 72(4):1011-5.

Andersen HR, Vinggaard AM, Rasmussen TH, Gjermandsen IM, Bonefeld-Jorgensen EC. 2002. Effects of currently used pesticides in assays for estrogenicity, androgenicity, and aromatase activity in vitro. *Toxicol Appl Pharmacol* 179(1):1-12.

Antherieu S, Ledirac N, Luzy AP, Lenormand P, Caron JC, Rahmani R. 2007. Endosulfan decreases cell growth and apoptosis in human HaCaT keratinocytes: Partial ROS-dependent ERK1/2 mechanism. *J Cell Physiol* 213(1):177-86.

Associated Press. 2007. Students sicken when pesticides drift. Tuesday May 15. Strathmore, California.

ATSDR. 2000. Toxicological Profile for Endosulfan. Agency of Toxic Substances and Disease Registry, Atlanta, USA. http://www.atsdr.cdc.gov/toxprofiles/tp41.html

Bajpayee M, Pandey AK, Zaidi S, Musarrat J, Parmar D, Mathur N, Serth PK, Dhawan A. 2006. DNA damage and mutagenicity induced by endosulfan and its metabolites. *Environ Mol Mutagen* 47(9):682-92.

Bastos CS, de Almeida RP, Suinaga FA. 2006. Selectivity of pesticides used on cotton (*Gossypium hirsutum*) to *Trichogramma* pretiosum reared on two laboratory-reared hosts. Pest Manag Sci 62:91–8.

Benamú MA, Schneider MI, Pineda S, Sanchez NE, Gonzalez A. 2007. Sublethal effects of two neurotoxican insecticides on Araneus pratensis (Araneae: Araneidae). *Commun Agric Appl Biol Sci* 72(3):557-9.

Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, Sciajno R, Pisani P, Panico S, Secreto G. 1996. Serum sex hormone levels after menopause and subsequent breast cancer. *J Natl Cancer Inst* 88:291-6.

Bollmohr S, Day JA, Schulz R. 2007. Temporal variability in particle-associated pesticide exposure in a temporarily open estuary, Western Cape, South Africa. *Chemosphere* 68:479-88.

Bonefeld-Jorgensen EC, Grunfeld HT, Gjermandsen IM. 2005. Effect of pesticides on estrogen receptor transactivation in vitro: a comparison of stable transfected MVLN and transient transfected MCF-7 cells. *Mol Cell Endocrinol* 244(1-2):20-30.

Bostanian NJ, Akalach M. 2004. The contact toxicity of indoxacarb and five other insecticides to *Orius insidiosus* (Hemiptera: Anthocoridae) and *Aphidius colemani* (Hymenoptera: Braconidae), beneficials used in the greenhouse industry. *Pest Manag Sci* 60(12):1231-6.

Bradlow HL, Davis DL, Lin G, Sepkovic D, Tiwari R. 1995. Effects of pesticides on the ratio of 16/2-hydroxyestrone: a biologic marker of breast cancer risk. *Environ Health Perspect* 103 (S-7):147-50.

Braune BM, Outridge PM, Fisk AT, Muir DCG, Helm PA, Hobbs K, Hoekstra PF, Kuzyk ZA, Kwan M, Letcher RJ, Lockhart WL, Norstrom RJ, Stern GA, Stirling I. 2005. Persistent organic pollutants and mercury in marine biota of the Canadian Arctic: an overview of spatial and temporal trends. *Sci Total Environ* 351-352: 4-56.

Brun GL, MacDonald RM, Verge J, Aube J. 2008. Long-term atmospheric deposition of current-use and banned pesticides in Atlantic Canada; 1980-2000. *Chemosphere* 71:314-27.

Cabaleiro T, Caride A, Romero A, Lafuente A. 2008. Effects of *in utero* and lactational exposure to endosulfan in prefrontal cortex of male rats. *Toxicol Letts* 176:58–67.

Campoy C, Jimenz M, Olea-Serrano MF, Moreno-Frias M, Canabate F, Olea N, Bayes R, Molina-Font JA. 2001. Analysis of organochlorine pesticides in human milk: preliminary results. *Early Hum Devel* 65(s2):S183-190.

Carlson DL, Basu I, Hites RA. 2004. Annual variations of pesticide concentrations in Great Lakes precipitation. *Environ Sci Technol* 38(20):5290-6.

Carreno J, Rivas A, Granada A, Lopez-Espinosa MJ, Mariscal M, Olea N, Olea-Serrano F. 2007. Exposure of young men to organochlorine pesticides in Southern Spain. *Environ Res* 103:55-61.

Carrera G, Fernandez P, Grimalt JO. 2002. Atmospheric deposition of organochlorine compounds to remote high mountain lakes of Europe. *Environ Sci Technol* 36:2581-8.

Cerrillo I, Granada A, Lopez-Espinosa MJ, Olmos B, Jimenez M, Cano A, Olea N, Fatima Olea-Serrano M. 2005. Endosulfan and its metabolites in fertile women, placenta, cord blood, and human milk. *Environ Res* 98(2):233-39.

Chatterjee S, Kumar V, Majumder CB, Roy P. 2008. Screening of some anti-progestin endocrine disruptors using a recombinant yeast-based in vitro bioassay. *Toxicol in Vitro* 22(3):788-98.

Cossette LJ, Gaumond I, Martinoli MG. 2002. Combined effect of xenoestrogens and growth factors in two estrogen-responsive cell lines. *Endocrine* 18(3):303-8.

Daly GL, Lei YD, Teixeira C, Muir DCG, Wania F. 2007a. Pesticides in western Canadian mountain air and soil. *Environ Sci Technol* 41:6020-5.

Damgaard IN, Skakkebaek NE, Toppari J, Virtanen HE, Shen H, Schramm KW, Petersen JH, Jensen TK, Main KM, Nordic Cryptorchidism Study Group. 2006. Persistent pesticides in human breast milk and cryptorchidism. *Environ Health Perspect*. 114(7):1133-8

Deger AB, Gremm TJ, Frimmel FH, Mendez L. 2003. Optimization and application of SPME for the gas chromatographic determination of endosulfan and its major metabolites in the ^{ngL-1} range in aqueous solutions. *Anal Bioanal Chem* 376:61-8.

Dorgan JF, Longcope C, Stephenson HE, Falk RT, Miller R, Franz C, Kahle L, Campbell WS, Tangrea JA, Schatzkin A. 1996. Relation of prediagnostic serum estrogen and androgen levels to breast cancer risk. *Cancer Epidemiol Biomark Prev* 5:533-9.

Dubois M, Pfohl-Leszkowicz A, De Waziers I, Kremers P. 1996. Selective induction of the CYP3A family by endosulfan and DNAadduct formation in different hepatic and hepatoma cells. *Environ Toxicol Pharmacol* 1(1):249-56.

EJF. 2002. End of the Road for Endosulfan: A Call For Action Against a Dangerous Pesticide. Environmental Justice Foundation, London. http://www.ejfoundation.org.

El Hindi AM, Dukeen MYH, Abdelbagi AO, Kafi HT, Ahamed AH, Mubark S, Ahmed FTA, Mawien R. 2006. Vector Control Needs Assessment. Draft Report prepared by the Sudan National VCNA Team, Kartoum.

Elzen GW. 2001. Lethal and sublethal effects of insecticide residues on *Orius insidiorus* (Hemiptera: Anthocoridae) and *Geocoris punctipes* (Hemiptera: Lygaeidae). *J Econ Entomol* 94(1):55-9.

ERMANZ. 2007b. Application for Reassessment of a Hazardous Substance under Section 63 of the Hazardous Substances and New Organisms Act 1996. Name of substance: Endosulfan and Formulations containing Endosulfan. Environmental Risk Management Authority of New Zealand, Wellington. <u>http://www.ermanz.govt.nz</u>.

Evans MS, Muir D, Lockhart WL, Stern G, Ryan M, Roach P. 2005. Persistent organic pollutants and metals in the freshwater biota of the Canadian Subarctic and Arctic: an overview. *Sci Total Environ* 351-352:94-147.

Fransson-Steen R, Flodstrom S, Warngard L. 1992. The insecticide endosulfan and its two stereoisomers promote the growth of altered hepatic foci in rats. *Carcinogenesis* 13(12):2299-303.

Fukata H, Omori M, Osada H, Todaka E, Mori C. 2005. Necessity to measure PCBs and organochlorine pesticide concentrations in human umbilical cords for fetal exposure assessment. *Environ Health Perspect* 113:297-303.

Garg UK, Pal AK, Jha GJ, Jadhao SB. 2004. Haemato-biochemical and immuno-pathophysiological effects of chronic toxicity with synthetic pyrethroid, organophosphate and chlorinated pesticides in broiler chicks. *Int Immunopharmacol* 4(13):1709-22.

Garrison VH, Foreman WT, Genualdi S, Griffin DW, Kellogg CA, Majewski MS, Mohammed A, Ramsubhag A, Shinn EA, Simonich SL, Smith GW. 2006. Saharan dust – a carrier of persistent organic pollutants, metals and microbes to the Caribbean? *Rev Biol Trop* 54(Suppl 3):9-21.

GEF CAC. 2002. Regionally Based Assessment of Persistent Toxic Substances – Central America and the Caribbean Regional Report. Global Environment Facility, United Nations Environmental Programme, Geneva. <u>http://www.chem.unep.ch/Pts/</u>.

GEF SSA. 2002. Regionally Based Assessment of Persistent Toxic Substances – Sub-Saharan Africa Regional Report. Global Environment Facility, United Nations Environmental Programme, Geneva. <u>http://www.chem.unep.ch/Pts/</u>.

GFEA-U. 2007. Endosulfan. Draft Dossier prepared in support of a proposal of endosulfan to be considered as a candidate for inclusion in the CLRTAP protocol on persistent organic pollutants. German Federal Environment Agency – Umweltbundesamt, Berlin.

Glin Lj, Kuiseau J, Thiam A, Vodouhe DS, Dinham B, Ferrigno S. 2006. *Living with Poison: Problems of Endosulfan in West Africa Cotton Growing Systems.* Pesticide Action Network UK, London.

Grunfeld HT, Bonefeld-Jorgensen EC. 2004. Effect of in vitro estrogenic pesticides on human oestrogen receptor alpha and beta mRNA levels. *Toxicol Lett* 151(3):467-80.

Hageman KJ, Simonich SL, Campbell DH, Wilson GR, Landers DH. 2006. Atmospheric deposition of current-use and historicuse pesticides in snow at national parks in the western United States. *Environ Sci Technol* 40:3174-80.

Herbert BMJ, Halsall CJ, Fitzpatrick L, Villa S, Jones KC, Thomas GO. 2004. Use and validation of novel snow samplers for hydrophobic, semi-volatile organic compounds (SVOCs). *Chemosphere* 56:227-35.

Hung H, Halsall CJ, Blanchard P, Li HH, Fellin P, Stern G, Rosenberg B. 2002. Temporal trends of organochlorine pesticides in the Canadian Arctic atmosphere. *Environ Sci Technol* 36(5):862-8.

Hung H, Blanchard P, Halsall CJ, Bidleman TF, Stern GA, Fellin P, Muir DC, Barrie LA, Jantunen LM, Helm PA, Ma J, Konoplev A. 2005. Temporal and spatial variabilities of atmospheric polychlorinated biphenyls (PCBs), organochlorine (OC) pesticides and

polycyclic aromatic hydrocarbons (PAHs) in the Canadian Arctic: results from a decade of monitoring. *Sci Total Environ* 342(1-3):119-44.

Jamil K, Shaik AP, Mahboob M, Krishna D. 2004. Effect of organophosphorus and organochlorine pesticides (monocrotophos, chlorpyriphos, dimethoate, and endosulfan) on human lymphocytes in-vitro. *Drug Chem Toxicol* 27(2):133-44.

Jayashree R, Vasudevan N. 2007b. Persistence and distribution of endosulfan under field conditions. *Environ Monit Assess* 131(1-3):475-87.

Je KH, Kim KN, Nam KW, Cho MH, Mar W. 2005. TERT mRNA expression is up-regulated in MCF-7 cells and a mouse mammary organ culture (MMOC) system by endosulfan treatment. *Arch Pharm Res* 28(3):351-7.

Jia Z, Misra HP. 2007a. Developmental exposure to pesticides zineb and/or endosulfan renders the nigrostriatal dopamine system more susceptible to these environmental chemicals later in life. *Neurotoxicology* 28(4):727-35.

Jonsson CM, Toledo MCF. 1993. Bioaccumulation and elimination of endosulfan in the fish yellow tetra (*Hypessobrycon bifasciatus*). Bull Environ Contam Toxicol 50:572-7.

Kannan K, Holcombe RF, Jain SK, Alvarez-Hernandez X, Chervenak R, Wolf RE, Glass J. 2000. Evidence for the induction of apoptosis by endosulfan in a human T-cell leukemic line. *Mol Cell Biochem* 205(1-2):53-66.

Kelly BC, Gobas FAPC. 2003. An arctic terrestrial food-chain bioaccumulation model for persistent organic pollutants. *Environ Sci Total* 37(13):2966-74.

Kelly BC, Ikonomou MG, Blair JD, Morin AE, Gobas FAPC. 2007. Food web-specific biomagnification of persistent organic pollutants. *Science* 317:236-9.

Kennedy IR, Sanchez-Bayo F, Kimber SW, Hugo L, Ahmad N. 2001. Off-site movement of endosulfan from irrigated cotton in New South Wales. *J Environ Qual* 30:683-96.

Kishi M. 2002. Initial Summary of the Main Factors Contributing to Incidents of Acute Pesticide Poisoning. Report to IFCS Forum Standing Committee Working Group.

Kojima H, Katsura E, Takeuchi S, Niiyama K, Kobayashi K. 2004. Screening for estrogen and androgen receptor activities in 200 pesticides by *in vitro* reporter gene assays using Chinese hamster ovary cells. *Environ Health Perspect* 112(5):524-31.

Kuang Z, McConnell LL, Torrents A, Meritt D, Tobash S. 2003. Atmospheric deposition of pesticides to an agricultural watershed of the Chesapeake Bay. *J Environ Qual* 32(5):1611-22.

Kumari B, Madan VK, Kathpal TS. 2007. Pesticide residues in rain water from Hisar, India. Environ Monit Assess 133:467-71.

Kuvarega AT, Taru P. 2007. Accumulation of endosulfan in wild rat, *Rattus norvegious* as a result of application to soya bean in Mazoe (Zimbabwe). *Environ Monit Assess* 125(1-3):333-45.

Laabs V, Amelung W, Pinto AA, Wantzen M, da Silva CJ, Zech W. 2002. Pesticides in surface water, sediment, and rainfall of the northeastern Pantanal Basin, Brazil. *J Environ Qual* 31:1636-48.

Laabs V, Wehrhan A, Pinto A, Dores E, Amelung W. 2007. Pesticide fate in tropical wetlands of Brazil: an aquatic microcosm study under semi-field conditions. *Chemosphere* 67:975–89.

Lafuente A, Cabaleiro T, Caride A, Romero A. 2006. Toxic effects of endosulfan on blood lymphocyte subset in adult rats. *Toxicol Letts* 164S:S234.

Lajmanovich RC, Cabagna M, Peltzer PM, Stringhini GA, Attademo AM. 2005. Micronucleus induction in erthrocytes of the *Hyla* pulchella tadpoles (Amphibia: Hylidae) exposed to insecticide endosulfan. *Mut Res* 587(1-2):67-72.

Landers DH, Simonich SL, Jaffe DA, Geiser LH, Campbell DH, Schwindt AR, Schreck CB, Kent ML, Hafner WD, Taylor HE, Hageman KJ, Usenko S, Ackerman LK, Schrlau JE, Rose NL, Blett TF, Erway MM. 2008. *The Fate, Transport, and Ecological Impacts of Airborne Contaminants in Western National Parks (USA)*. EPA/600/R-07/138. U.S. Environmental Protection Agency, Office of Research and Development, NHEERL, Western Ecology Division, Corvallis, Oregon.

Laville N, Balguerf P, Brion F, Hinfray N, Casellas C, Porcher JM, Ait-Aissa S. 2006. Modulation of aromatase and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line. *Toxicology* 228(1):98-108.

Lemaire G, Mnif W, Mauvais P, Balaguer P, Rahmani R. 2006. Activation of alpha- and beta-estrogen receptors by persistent pesticides in reporter cell lines. *Life Sci* 79(12):1160-9.

Lu Y, Morimoto K, Takeshita T, Takeuchi T, Saito T. 2000. Genotoxic effects of alpha-endosulfan and beta-endosulfan on human HepG2 cells. *Environ Health Perspect* 108(6):559–561.

Mast MA, Foreman WT, Skaates SV. 2007. Current-use pesticides and organochlorine compounds in precipitation and lake sediment from two high-elevation national parks in the western United States. *Arch Environ Contam Toxicol* 52:294-305.

Menone ML, Aizpun de Moreno JE, Moreno VJ, Lanfranchi AL, Metcalfe TL, Metcalfe CD. 2000. PCBs and organochlorines in tissues of silverside (*Odontesthes bonariensis*) from a coastal lagoon in Argentina. *Arch Environ Contam Toxicol* 38:202-8.

Menone ML, Pesce SF, DI^{az} MP, Moreno VJ, Wunderlin DA. 2008. Endosulfan induces oxidative stress and changes on detoxication enzymes in the aquatic macrophyte Myriophyllum quitense. *Phytochemistry* 69(5):1150-7.

Miglioranza KS, de Moreno JE, Moreno VJ. 2004b. Organochlorine pesticides sequestered in the aquatic macrophyte Schoenoplectus californicus (C.A. Meyer) Sojak from a shallow lake in Argentina. *Water Res* 38(7):1765-72.

Mingxin B (ed). 2007. Pesticide kills farmer, poisons 154. English News Service, Xinhua News Agency, China. Aug 3. http://news.xinhuanet.com/english/2007-08/04/content 6471548.htm.

Miranda-Filho KC, Metcalfe TL, Metcalfe CD, Robaldo RB, Muelbert MMC, Colares EP, Martinez PE, Bianchini A. 2007. Residues of persistent organochlorine contaminants in southern elephant seals (*Mirounga leonina*) from Elephant Island, Antarctica. *Environ Sci Technol* 41:3829-35.

Narita S, Goldblum RM, Watson CS, Brooks EG, Estes DM, Curran EM, Midoro-Horiuti T. 2007. Environmental estrogens induce mast cell degranulation and enhance IgE-mediated release of allergic mediators. *Environ Health Perspect* 115(1):48-52.

NCP. 2003. Canadian Arctic Contaminants Assessment Report II: Highlights. Northern Contaminants Programme, Indian and Northern Affairs Canada, Ottawa.

Neuparth T, Bickham JW, Theodorakis CW, Costa FO, Costa MH. 2006. Endosulfan-induced genotoxicity detected in the Gilthead Seabream, *Sparus aurata* L., by means of flow cytometry and micronuclei assays. *Bull Environ Contam Toxicol* 76(2):242-8.

NIOH. 2003. Final Report of the Investigation of Unusual Illnesses Allegedly Produced by Endosulfan Exposure In Padre Village of Kasargod District (N Kerala). National Institute of Occupational Health, Indian Council for Medical Research, Ahmedabad.

Oktay C, Goksu E, Bozdemir N, Soyuncu S. 2003. Unintentional toxicity due to endosulfan: a case report of two patients and characteristics of endosulfan toxicity. *Vet Hum Toxicol* 45(6):318-20.

Omurtag GZ, Tozan A, Sehirli AO, Sener G. 2008. Melatonin protects against endosulfan-induced oxidative tissue damage in rats. *J Pineal Res* 42(4):386-93.

Pandey N, Gundevia F, Prem AS, Ray PK. 1990. Studies on the genotoxicity of endosulfan, an organochlorine insecticide, in mammalian germ cells. *Mutat Res* 242(1):1-7.

Pandey S, Nagpure NS, Kumar R, Sharma S, Srivastava SK, Verma MS. 2006. Genotoxicity evaluation of acute doses of endosulfan to freshwater teleost *Channa punctatus* (Bloch) by alkaline single-cell gel electrophoresis. *Ecotoxicol Environ Saf* 65(1):56-61.

PANNA. 1996. Endosulfan responsible for Alabama fish kill. PANUPS. Pesticide Action Network North America. http://www.panna.org.

PANNA. 1999. Pesticide poisoning in Cuba. Global Pesticide Monitor 9(2):28.

Pathak R, Suke SG, Ahmed RS, Tripathi AK, Guleria K, Sharma CS, Makhijani SD, Mishra M, Banerjee. 2008. Endosulfan and other organochlorine pesticide residues in maternal and cord blood in North Indian population. Bull *Environ Contam Toxicol* May 17 [Epub ahead of print].

Perez DJ, Menone ML, Camadro EL, Moreno VJ. 2007. Genotoxicity evaluation of the insecticide endosulfan in the wetland macrophyte *Bidens laevis* L. *Environ Pol* 153(3):695-8.

Pistl J, Kovalkovicova N, Holovska V, Legath J, Mikula I. 2003. Determination of the immunotoxic potential of pesticides on functional activity of sheep leukocytes in vitro. *Toxicology* 188(1):73-81.

Pozo K, Harner T, Wania F, Muir DCG, KC, Barrie LA. 2006. Toward a global network for persistent organic pollutants in air: Results from the GAPS study. *Environ Sci Technol* 40(16):4867-73.

Pradhan S, Pandey N, Phadke RV, Kaur A, Sharma K, Gupta RK. 1997. Selective involvement of basal ganglia and occipital cortex in a patient with acute endosulfan poisoning. *J Neurol Sci* 147(2):209-13.

Quaghebeur D, De Smet B, De Wulf E, Steurbaut W. 2004. Pesticides in rainwater in Flanders, Belgium: results from the monitoring program 1997-2001. *J Environ Monit* 6(3):182-90.

Quijano RF. 2002. Endosulfan Poisoning in Kasargod, Kerala, India: Report on a Fact-Finding Mission. Pesticide Action Network Asia and the Pacific, Penang.

Roberts DM, Dissanayake W, Sheriff MHR, Eddeston M. 2004. Refractory status epilepticus follow self-poisoning with the organochlorine pesticide endosulfan. *J Clin Neurosci* 11(7):760-62.

Roberts EM, English PB, Grether KJ, Windham GC, Somberg L, Wolff C. 2007. Maternal residence near agricultural pesticide applications and autism spectrum disorders among children in the California Central Valley. *Environ Health Perspect* 115(10):1482-9.

Rousseau J, Cossette L, Grenier S, Martinoli MG. 2002. Modulation of prolactin expression by xenoestrogens. *Gen Comp Endocrinol* 126(2):175-82.

Sanghi R, Pillai MK, Jayalekshmi TR, Nair A. 2003. Organochlorine and organophosphorus pesticide residues in breast milk from Bhopal, Madhya Pradesh, India. *Hum Exp Toxicol* 22(2):73-6.

Saiyed H, Dewan A, Bhatnagar V, Shenoy U, Shenoy R, Rajmohan H, Patel K, Kashyap R, Kulkarni P, Rajan B, Lakkad B. 2003. Effect of endosulfan on male reproductive development. *Environ Health Perspect* 111(16):1958-62.

Scheyer A, Morville S, Mirabel P, Millet M. 2007. Pesticides analysed in rainwater in Alsace region (Eastern France): Comparison between urban and rural sites. *Atmos Environ* 41(34):7241-52.

Schneider MI, Pineda P, Smagghe G. 2006. Side effects of conventional and non-conventional insecticides on eggs and larvae of *Chrysoperla externa* (Hagen) (Neuroptera: Chrysopidae) in Argentine. *Commun Agric Appl Biol Sci* 71(2 Pt B):425-7.

Schulz R. 2004. Field studies on exposure, effects, and risk mitigation of aquatic nonpoint-source insecticide pollution: a review. J Environ Qual 33(2):419-48.

Sharma S, Nagpure NS, Kumar R, Pandey S, Srivastava SK, Singh PJ, Mathur PK. 2007a. Studies on the genotoxicity of endosulfan in different tissues of fresh water fish *Mystus vittatus* using the Comet assay. *Arch Environ Contam Toxicol* 53(4):617-23.

Shen H, Main KM, Virtanen HE, Damgaard IN, Haavisto A-M, Kaleva M, Boisen KA, Schmidt IM, Chellakooty M, Skakkebaek NE, Toppari J, Schramm K-W. 2007. From mother to child: investigation of prenatal and postnatal exposure to persistent bioaccumulating toxicants using breast milk and placenta biomonitoring. *Chemosphere* 67:S256-62.

Shen H, Main KM, Andersson A-M, Damgaard IN, Virtanen HE, Skakkebaek NE, Toppari J, Schramm K-W. 2008. Concentrations of persistent organochlorine compounds in human milk and placenta are higher in Denmark than in Finland. *Hum Reprod* 23(1):201-10.

Singh ND, Sharma AK, Dwivedi P. Patil RD, Kumar M. 2006. Citrinin and endosulfan induced teratogenic effects in Wistar rats. J Appl Toxicol 27(6):589-601.

Sobti RC, Krishan A, Davies J. 1983. Cytokinetic and cytogenetic effect of agricultural chemicals on human lymphoid cells in vitro II. Organochlorine pesticides. *Arch Toxicol* 52:221-31.

Soto AM, Chung KL, Sonnenschein C. 1994. The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells. *Environ Health Perspect* 102(4):380-83.

Soto AM, Sonnenschein C, Chung KL, Fernandez MF, Olea N, Serrano FO. 1995. The E-SCREEN assay as a tool to identify estrogens: an update on estrogenic environmental pollutants. *Environ Health Perspect* 103(Suppl 7):113-22.

Stern GA, Macdonald CR, Armstrong D, Dunn B, Fuchs C, Harwood L, Muir DCG, Rosenburg B. 2005. Spatial trends and factors affecting variation of organochlorine contaminants levels in Canadian Arctic beluga (*Delphinapterus leucas*). *Sci Total Environ* 351-352:344-68.

Sun P, Backus S, Blanchard P, Hites RA. 2006. Temporal and spatial trends of organochlorine pesticides in Great Lakes precipitation. *Environ Sci Technol* 40:2135-41.

Sutherland TD, Home I, Weir KM, Russell RJ, Oakeshott JG. 2004. Toxicity and residues of endosulfan isomers. *Rev Environ Contam Toxicol* 183:99-113.

Ton P. 2000. Endosulfan deaths in Benin. Pesticides News 48:17.

Toniolo PG, Levitz M, Zeleniuch-Jacquotte A, Banerjee S, Koenig KL, Shore RE, Strax P, Pasternack BS. 1995. A prospective study of endogenous estrogens and breast cancer in postmenopausal women. *J Natl Cancer Inst* 87:190-7.

Torres MJ, Folgoso CC, Reche FC, Velasco AR, Garcia IC, Arcas MM, Olea-Serrano F. 2006. Organochlorine pesticides in serum and adipose tissue of pregnant women in Southern Spain giving birth by cesarean section. *Sci Total Environ* 372(1):32-8.

Tuduri L, Harner T, Blanchard P, Li Y-F, Poissant L, Waite DT, Murphy C, Belzer W. 2006. A review of currently used pesticides (CUPs) in Canadian air and precipitation: Part 1: Lindane and endosulfans. *Atmos Environ* 40:1563-78.

US EPA. 2007c. Addendum to the Ecological Risk Assessment for Endosulfan. Memorandum to Special Review and Reregistration Branch. Oct 31. EPA-HQ-OPP-2002-0262-0063. <u>http://www.regulations.gov</u>.

Venkateswarlu K, Suryarao K, Srinivas V, Sivaprakash N, Jagannadharao NR, Mythilai A. 2000. Endosulfan poisoning – a clinical profile. *J Assoc Physicians India* 48(3):323-5. Cited in Kishi 2002.

Venugopal PN. 2008. Endosulfan victims still suffer in India. Feb 15. http://southasia.oneworld.net/article/view/157876/1.

Vig K, Singh DK, Agarwal HC, Dhawan AK, Dureja P. 2008. Soil microorganisms in cotton fields sequentially treated with insecticides. *Ecotoxicol Environ Saf* 69(2):263-76.

Vorkamp K, Riget F, Glasius M, Pecseli M, Lebeuf M, Muir D. 2004. Chlorobenzenes, chlorinated pesticides, coplanar chlorobiphenyls and other organochlorine compounds in Greenland biota. *Sci Total Environ* 331(1-3):157-75.

Wang XF, Li S, Chou AP, Bronstein JM. 2006a. Inhibitory effects of pesticides on proteasome activity: implication in Parkinson's disease. *Neurobiol Dis* 23(1):198-205.

Wang X-p, Yao T-d, Cong Z-d, Yan X-I, Kang S-c, Zhang Y. 2006b. Gradient distribution of persistent organic contaminants along northern slope of central-Himalayas, China. *Sci Total Environ* 372:193-202.

Wang XP, Yao TD, Cong ZY, Yan XL, Kang SC, Zhang Y. 2007a. Distribution of persistent organic pollutants in soil and grasses around Mt. Qomolangma, China. Arch Environ Contam Toxicol 52(2):1530-62.

Warngard I, Bager Y, Kato Y, Kenne K, Ahlborg UG. 1996. Mechanistical studies of the inhibition of intercellular communication by organochlorine compounds. *Arch Toxicol Suppl* 18:149-59.

Wessel N, Rousseau S, Caisey X, Quiniou F, Akcha F. 2007. Investigating the relationship between embryotoxic and genotoxic effects of benzo[a]pyrene, 17*a*-ethinylestradiol and endosulfan on *Crassostrea gigas* embryos. *Aquat Toxicol* 85:133-42.

Wesseling C, Corriols M, Bravo V. 2005. Acute pesticide poisoning and pesticide registration in Central America. *Toxicol Appl Pharmacol* 207(2 Suppl 1):697-705.

Wong PS, Matsumura F. 2006. Serum free BG-1 cell proliferation assay: a sensitive method for determining organochlorine pesticide estrogen receptor activation at the nanomolar range. *Toxicol In Vitro* 20(3):382-94.

Wozniak AL, Bulayeva NN, Watson CS. 2005. Xenoestrogens at picomolar to nanomolar concentrations trigger membrane estrogen receptor-alpha-mediated Ca²+ fluxes and prolactin release in GH3/B6 pituitary tumor cells. *Environ Health Perspect* 113(4):431-9.

Yadav AS, Vashishat RK, Kakar SN. 1982. Testing of endosulfan and fenitrothion for genotoxicity in *Saccharomyces cerevisiae*. *Mutat Res* 105(6):403-7.