Format for submitting pursuant to Article 8 of the Stockholm Convention the information specified in Annex E of the Convention

Introductory information

Name of the submitting Party/observer

NGO Observer: Pesticide Action Network on behalf of the International POPs Elimination Network (IPEN)

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Chemical name

Chlordecone

Chemical name: 1,1a,3,3a,4,5,5,5a,5b,6-decachloro-octahydro-1,3,4-metheno-2H-cyclobuta[cd]pentalen-2-one

CAS=143-50-0

Common trade names: GC 1189, Kepone, Merex

Synonyms: Chlordecone, Chlordecone Kepone, Decachloroketone, Decachlorooctahydro-1,3,4-metheno-2H-cyclobuta(cd)pentalen-2-one, Decachloropentacyclo(5.3.0.0.0.0 2,6,4,10,5,9)decane-3-one, Decachlorotetracyclodecanone
decachlorooctahydro- ,

Date of submission

27 January 2006

(a) Sources, including as appropriate **(provide summary information and relevant references)**

(i) Production data:

Quantity

[1] "Chlordecone is no longer produced commercially in the United States. Between 1951 and 1975, approximately 3.6 million pounds (1.6 million kg) of chlordecone were produced in the United States (Epstein 1978). During this period, Allied Chemical

Company produced approximately 1.8 million pounds (816,500 kg) of chlordecone at plants in Claymont, Delaware; Marcus Hook, Pennsylvania and Hopewell, Virginia. In 1974, because of increasing demand for chlordecone and a need to use their facility in Hopewell, Virginia, for other purposes, Allied Chemical transferred its chlordecone manufacturing to Life Sciences Products Company (EPA 1978b). Life Sciences Products produced an estimated 1.7 million pounds (771,000 kg) of chlordecone from November 1974 through July 1975 in Hopewell, Virginia (Epstein 1978). Hooker Chemical Company also produced approximately 49,680 (22,500 kg) pounds of chlordecone in the period from 1965 to 1967 at a plant at Niagara Falls, New York. Nease Chemical Company produced approximately 65,780 pounds (30,000 kg) of chlordecone between 1959 and 1966 at a plant in State College, Pennsylvania (Epstein 1978)." (Agency for Toxic Substances and Disease Registry, USA Department of Health and Human Services. Toxicological profile for mirex and chlordecone. August 1995)

Location

See above

(ii) Uses

[2] "Until August 1, 1976, chlordecone was registered in the United States for use on banana root borer (in the U.S. territory of Puerto Rico); this was its only registered food use. Additional registered formulations included non-food use on non-fruit bearing citrus trees to control rust mites; on tobacco to control tobacco and potato wireworms; and for control of the grass mole cricket, and various slugs, snails, and fire ants in buildings, lawns, and on ornamental shrubs (EPA 1978b; Epstein 1978; IARC 1979a). The highest reported concentration of chlordecone in a commercial product was 50%, which was used to control the grass mole cricket in Florida (Epstein 1978). Chlordecone has also been used in household products such as ant and roach traps at concentrations of approximately 0.125% (IARC 1979a). The concentration used in ant and roach bait was approximately 25% (Epstein 1978). All registered products containing chlordecone were effectively canceled as of May 1, 1978 (Sittig 1980)." (Agency for Toxic Substances and Disease Registry, USA Department of Health and Human Services. Toxicological profile for mirex and chlordecone. August 1995)

(iii) Releases

Discharges

[3] "Major releases of chlordecone occurred to the air, surface waters, and soil surrounding a major manufacturing site in Hopewell, Virginia [USA]. Releases from this plant ultimately contaminated the water, sediment, and biota of the James River, a tributary to the Chesapeake Bay…In 1978, chlordecone was detected in sediments from the James River below its production site at concentrations in the mg/kg (ppm) range." (Agency for Toxic Substances and Disease Registry, USA Department of Health and Human Services. Toxicological profile for mirex and chlordecone. August 1995)

(b) Hazard assessment for endpoints of concern, including consideration of toxicological interactions involving multiple chemicals **(provide summary information and relevant references)**

General

[4] Recent contamination of the James River Estuary, Virginia, with Kepone prompted acute flow-through bioassays to determine the 96-hour toxicity of the insecticide to four estuarine species native to that ecosystem. The species and their 96-hour LC50 values were: grass shrimp (Palaemonetes pugio), 121 µg/liter; blue crab (Callinectes sapidus) >210 µg/liter; sheepshead minnow (Cyprinodon variegatus),, 69.5 µg/liter; and spot (Leiostomus xanthurus) 6.6 µg/liter. Surviving animals were analyzed for Kepone. Average bioconcentration factors (the concentration of Kepone in tissues divided by the concentration of Kepone measured in seawater) were: grass shrimp, 698; blue crab, 8.1; sheepshead minnow, 1,548; and spot, 1,221.
Schimmel, Steven C. and Alfred J. Wilson, Jr. 1977. Acute Toxicity of Kepone to Four Estuarine Animals. Chesapeake Sci. 18(2):224-227. (ERL,GB 293).

Endocrine Disruption

[5] **Categorised as endocrine disruptor**
Agreed by the German Environment Agency, the European Union, OSPAR and WWF to be an endocrine disrupting Pesticide Action Network. The EU category 1 is based on "At least one study providing evidence of endocrine disruption in an intact organism. Not a formal weight of evidence approach."

[6] Two estrogenic actions, initiation of implantation and maintenance of pregnancy, were examined in progesterone-primed, delayed-implanting, hypophysectomized rats exposed to several polychlorinated hydrocarbons. Chlordecone (Kepone) was more estrogenic than any of the DDT analogs and maintained pregnancy with a single dose of 50 mg/kg.
DC Johnson, M Sen and SK Dey, Differential effects of dichlorodiphenyltrichloroethane analogs, chlordecone, and 2,3,7,8-tetrachlorodibenzo-p-dioxin on establishment of pregnancy in the hypophysectomized rat, Proceedings of the Society for Experimental Biology and Medicine, Vol 199, 42-48, Society for Experimental Biology and Medicine

[7] The effects of chlordecone (Kepone) on rat uterine estrogen receptor were examined *in vitro* and *in vivo*. In cell free preparations, chlordecone was found to inhibit the binding of [^{3}H]estradiol to uterine cytosolic 8S estrogen receptor in a competitive manner, suggesting that chlordecone binds to the same site as estradiol. Incubation of isolated uteri *in vitro* in the presence of chlordecone resulted in an increrase in estrogen receptor in the nuclear fraction. This increase accompanied a decline in the amount of estrogen receptor in the cytosolic fraction, indicating that translocation of the estrogen receptor had occurred.
Bulger WH [1], Muccitelli, RM[1], and Kupfer D[1]. Studies on the Estrogenic Activity of Chlordecone (Kepone) in the Rat: Effects on Uterine Estrogen Receptor Molecular

Pharmacology, Vol 15, 515-524, American Society for Pharmacology and Experimental Therapeutics

[8] Because the adverse impacts on crustacean molting cannot be readily seen in the wild, the disruption of molting represents an invisible form of endocrine disruption.
Zou E, Impacts of Xenobiotics on Crustacean Molting: The Invisible Endocrine Disruption, Integrative and Comparative Biology, February 2005.
Blue crabs, Callinectes sapidus, fed oysters contaminated with kepone, molt less frequently than crabs fed kepone-free oysters *Schimmel, S. C., J. M. Patrick, Jr., L. E Faas, J. L. Oglesby, and A. J. Wilson, Jr. 1979. Kepone: Toxicity and bioaccumulation in blue crabs. Estuaries 2:9-15.*

[9] Chlordecone, …. had capacities to bind both ERalpha and AR. Chlordecone and pyridate were much more effective as competitors of estrogen binding to ERalpha than androgen binding to AR
Okubo T, Yokoyama Y, Kano K, Soya Y and Kano I. Estimation of estrogenic and antiestrogenic activities of selected pesticides by MCF-7 cell proliferation assay, Archives of Environmental Contamination and Toxicology, 2004, Vol 46, 445-453.

Cancer
[10] Chlordecone is listed in EU Category 3 – Possible risk of irreversible effects.
Directive 67/548/EEC on classification, packaging and labelling of dangerous substances, http://europa.eu.int/comm/environment/waste/studies/pdf/annex_4_physico_chem_properties.xls

IARC 2B – Possibly carcinogenic to humans. "There is *sufficient evidence* that chlordecone is carcinogenic in mice and rats. In the absence of adequate data in humans, it is reasonable, for practical purposes, to regard chlordecone as if it presented a carcinogenic risk to humans."
Overall Evaluations of Carcinogenicity to Humans, as evaluated in IARC Monographs Volumes 1-88 (Vol. 20, Suppl. 7; 1987) http://monographs.iarc.fr/monoeval/crthgr02b.html

[11] This study found a significant difference in the incidence of malignant liver tumors in Sprague – Dawley rats in females. Hepatocellular carcinomas were observed in up to 63% of the female rats that had been previously initiated with a subcarcinogenic dose of diethylnitrosamine and then promoted by 27 weeks of chlordecone administration. None of the comparably treated males showed this result. (Sirica AE , Wilkerson CS , Wu LL, Fitzgerald R, Blanke RV, Guzelian PS. Department of Pharmacology and Toxicology Richmond, VA, USA and Division of Clinical Toxicology and Environmental Medicine, Department of Internal Medicine, Medical College of Virginia, Virginia Commonwealth University Richmond, VA 23298, USA. Evaluation of chlordecone in a two-stage model of hepatocarcinogenesis: a significant sex difference in the hepatocellular carcinoma incidence, Carcinogenisis, 10:1047-1054, June 1989)

Immunotoxicity
[12] "Chlordecone treatment in (NZBxNZW) F(1) [ovary intact] mice shortened significantly the time to onset of elevated autoantibody titers and renal disease in a dose-related manner. The doses required to produce this effect were similar to those observed previously to accelerate SLE [systemic lupus erythematosus] development in ovariectomized females. Treatment of female BALB/c mice with chlordecone for up to

one year did not produce elevated autoantibody titers or renal disease, suggesting an inability of chlordecone to cause a break in tolerance in this strain. These observations confirm the ability of chronic chlordecone to influence SLE, but demonstrate the importance of genetic background for this effect." (Sobel ES, Wang F, Butfiloski F, Croker B, Roberts SM. Department of Medicine, J. Hillis Miller Health Science Center, University of Florida, USA. Comparison of chlordecone effects on autoimmunity in (NZBxNZW) F(1) and BALB/c mice. Toxicology 218:81-89, February 2006)

[13] Systemic lupus erythematosus (SLE) is an autoimmune disorder that affects women more frequently than men. In the (NZB x NZW)[F.sub.1] mouse, a murine SLE model, the presence or absence of estrogen markedly influences the rate of progression of disease. Three organochlorine pesticides with estrogenic effects were administered chronically to ovariectomized female (NZB x NZW)[F.sub.1] mice, and we measured the time to development of renal disease, the principal clinical manifestation of lupus in this model. Treatment with chlordecone, methoxychlor, or o,p'-dichlorodiphenyltrichloroethane (o,p'-DDT) significantly decreased the time to onset of renal impairment. In an expanded study of chlordecone, we found a dose-related early appearance of elevated anti-double-strand DNA autoantibody titers that corresponded with subsequent development of glomerulonephritis.
Eric S. Sobel, John Gianini, Edward J. Butfiloski, Byron P. Croker, Joel Schiffenbauer, Stephen M. Roberts. Acceleration of autoimmunity by organochlorine pesticides in [F.sub.1] mice. Environmental Health Perspectives March, 2005.

Neurotoxicity

[14] Twenty-three workers chronically exposed to chlordecone developed overt neurologic manifestations. These included postural and intention tremor, gait difficulty and opsoclonus. Blood levels of chlordecone ranged from 2.0 to 33.0 ppm. The manifestations slowly cleared in all but one worker.
Taylor JR. Neurological manifestations in humans exposed to chlordecone: follow-up results. Neurotoxicology,1985 Spring;6(1):231-6.

[15] Chlordecone is an organochlorine insecticide which intoxicated a number of workers in 1975 because of excessive exposure in the industrial plant. The major manifestations were tremor, opsoclonus, arthralgias, pleural pain, and reduced sperm count.
Taylor JR, Neurological manifestations in humans exposed to chlordecone and follow-up results, Neurotoxicology,1982 Oct;3(2):9-16.

[16] Industrial overexposure to chlordecone, an organochlorine insecticide, caused tremor in 76 of 148 exposed workers. Chlordecone was absorbed through oral, respiratory, and dermal routes, the last possibly the most significant. Epidemiology of this incident disclosed low-level, widespread environmental exposure of man to chlordecone. In 23 workers with chronic chlordecone intoxication, tremor was associated with opsoclonus, pleuritic pain and arthralgia. No seizures were reported. The site of action of chlordecone on the central nervous system is unknown. It concentrates in human adipose and hepatic tissue but is not biodegradable, either in humans or elsewhere in nature.
Taylor JR, Selhorst JB, Houff SA, Martinez AJ, Chlordecone intoxication in man. I. Clinical observations, Neurology, 1978 Jul;28(7):626-30

Epidemiology
[17] From March 1974 through July 1975, 76 (56%) of 133 persons who had worked at a pesticide plant that produced Kepone, a chlorinated hydrocarbon insecticide, contracted a previously unrecognized clinical illness characterized by nervousness, tremor, weight loss, opsoclonus, pleuritic and joint pain, and oligospermia. Illness incidence rates for production workers (64%) were significantly higher than for nonproduction personnel (16%).. Illness attributable to Kepone was found in two wives of Kepone workers; there was no apparent association between frequency of symptoms and proximity to the plant in the survey of the community population.
Cannon SB, Veazey JM Jr, Jackson RS, Burse VW, Hayes C, Straub WE, Landrigan PJ, Liddle JA, Epidemic kepone poisoning in chemical workers, Am J Epidemiol, 1978 Jun;107(6):529-37.

Reproductive
[18] Embryonic development, hatching, and survival and growth of fry and juveniles were monitored in a 36-day exposure to Kepone concentrations of 0.08, 0.18, 0.72, 2.0, 6.6, and 33 µg/liter. A significant number of embryos from adult fish exposed to 1.9 µg of Kepone/liter of water developed abnormally and died even when incubated in Kepone-free water. Kepone in water was not as lethal to progeny as to adults: 36-day LC50 for juveniles was 6.7 µg/liter; 28-day LC50 for adults, 1.3 µg/liter. However, the average standard length of juvenile fish was significantly reduced by exposure to 0.08 µg of Kepone/liter of water; some fish developed scoliosis. Concentration factors in juvenile sheepshead minnows averaged 7,200 and increased from 3,600 to 20,000 as exposure concentrations decreased.
Hansen, David J., Larry R. Goodman and Alfred J. Wilson, Jr. 1977. Kepone: Chronic Effects on Embryo, Fry, Juvenile, and Adult Sheepshead Minnows (Cyprinodon variegatus). Chesapeake Sci. 18(2):227-232. (ERL,GB 295).

(c) Environmental fate **(provide summary information and relevant references)**

Chemical/physical properties
Apparent colour – crystals; tan-to-white solid
Odourless
Non-combustible
Molecular weight: 490.68
Melting point: 350 Celsius (sublimes)
Solubility (at 100 Celsius) 0.5%

Please see also POPRC1-INF-6-w-anx

Persistence

AQUATIC FATE: If released to water, chlordecone will be expected to adsorb to the sediment.. It will not be expected to hydrolyze, biodegrade, or appreciably evaporate. (A half-life of 3.8-46 years has been predicted for evaporation from a river 1 m deep,

flowing at 1 m/sec with a wind velocity of 3 m/sec.) No data were found concerning the photodegradation of chlordecone irradiated at environmentally significant wavelengths. No significant direct photodegradation is expected. Chlordecone and mirex are among the most stable pesticides in the aquatic environment. After 56 days of incubation under both aerobic and anaerobic conditions, there was no evidence of degradation.
ATMOSPHERIC FATE: If chlordecone is released to the air, it will not be expected to directly photodegrade or to react with photochemically produced hydroxyl radicals or ozone. However, chlordecone should absorb to particulate matter and be subject to gravitational settling.
http://www.speclab.com/compound/c143500.htm

How are chemical/physical properties and persistence linked to environmental transport, transfer within and between environmental compartments, degradation and transformation to other chemicals?

[19] Chlordecone released to soil will be expected to adsorb to the soil; However, some leaching to the groundwater may occur, especially in sandy soils and other soils with low organic content. Biodegradation and hydrolysis will not be important fate processes but some evaporation may be observed from the surface of the soil. Chlordecone released to the water will be expected to adsorb to the sediment. Evaporation from water also should not be significant, with a half-life of 3.8-46 years predicted for evaporation from a river 1 m deep, flowing at 1 m/sec with a wind velocity of 3 m/sec.

Chlordecone released to the atmosphere will not be expected to react with photochemically produced hydroxyl radicals or ozone and will not be subject to appreciable direct photodegradation. Chlordecone should be sorbed to particulate matter in the atmosphere and thus subject to gravitational settling.
http://www.speclab.com/compound/c143500.htm

Please see also POPRC1-INF-6-w-anx

Bio-concentration or bio-accumulation factor, based on measured values (unless monitoring data are judged to meet this need)

[20] Accumulation, transfer, and loss of Kepone in estuarine organisms were studied in laboratory bioassays. Kepone was bioconcentrated by oysters (Crassostrea virginica), Mysids (Mysidopsis bahia), grass shrimp (Palaemonetes pugio), sheepshead minnows (Cyprinodon variegatus), and spot (Leiostomus xanthurus), from concentrations as low as 0.023 µg/l seawater. Bioconcentration factors ranged from 10 to 340 in static exposures and 900 to 13,500 in flow-through bioassays, and were dependent on species and exposure duration. Bioaccumulation factors (concentration of Kepone in predator/concentration in prey) at 30 days were equal (0.85 spot/mysid; 0.53 mysid/brine shrimp) in the high and low concentrations tested. The initial bioconcentration of Kepone from water by plankton was the dominant source of Kepone to each member of this food chain, but significant (>85%) quantities of Kepone transferred from prey to predatory fish.
Bahner, Lowell H., Alfred J. Wilson, Jr., James M. Sheppard, James M. Patrick, Jr., Larry R. Goodman and Gerald E. Walsh. 1977. Kepone Bioconcentration, Accumulation, Loss, and

Transfer Through Estuarine Food Chains. EPA-600/J-77-074. Chesapeake Sci. 18(3):299-308. (ERL,GB 294). (Avail. from NTIS, Springfield, VA: PB-277 183)

[21]Average bioconcentration factors (the concentration of Kepone in tissues divided by the concentration of Kepone measured in seawater) were: grass shrimp, 698; blue crab, 8.1; sheepshead minnow, 1,548; and spot, 1,221.
Schimmel, Steven C. and Alfred J. Wilson, Jr. 1977. Acute Toxicity of Kepone to Four Estuarine Animals. Chesapeake Sci. 18(2):224-227. (ERL,GB 293).

Please see also POPRC1-INF-6-w-anx

(d) Monitoring data **(provide summary information and relevant references)**

Human
22 The mean blood Kepone level for workers with illness was 2.53 ppm and for those without disease 0.60 ppm (p less than 0.001). Blood Kepone levels in current workers (mean, 3.12 ppm) were higher than those in former employees (1.22 ppm). Blood Kepone levels for workers in nearby businesses and for residents of a community within 1.6 km of the plant ranged from undetectable to 32.5 ppb. Illness attributable to Kepone was found in two wives of Kepone workers; there was no apparent association between frequency of symptoms and proximity to the plant in the survey of the community population.
Cannon SB, Veazey JM Jr, Jackson RS, Burse VW, Hayes C, Straub WE, Landrigan PJ, Liddle JA, Epidemic kepone poisoning in chemical workers, Am J Epidemiol, 1978 Jun;107(6):529-37.

Animal
[23] "Chlordecone has been detected in fish and shellfish from the James River, which empties into the Chesapeake Bay, at levels in the µg/g (ppm) range. There is currently a fish consumption advisory in effect for the lower 113 miles of the James River [USA]." (Agency for Toxic Substances and Disease Registry, USA Department of Health and Human Services. Toxicological profile for mirex and chlordecone. August 1995)

Coastline
[24] Agricultural pesticides were monitored on the coastline of Martinique where banana production uses large amounts of pesticides. "The organochlorine chlordecone and metabolites of aldicarb were detected at nearly all of the monitored sites, even though the use of chlordecone has been prohibited since 1993." (Bocquene G, Franco A. IFREMER, Rue de l'Ile d'Yeu, BP 21105, 44311 Nantes Cedex 3, France. Pesticide contamination of the coastline of Martinique. Mar Pollut Bull 51:612-619, July 2005)

(e) Exposure in local areas **(provide summary information and relevant references)**

- general
25 The mean blood Kepone level for workers with illness was 2.53 ppm and for those without disease 0.60 ppm (p less than 0.001). Blood Kepone levels in current workers

(mean, 3.12 ppm) were higher than those in former employees (1.22 ppm). Blood Kepone levels for workers in nearby businesses and for residents of a community within 1.6 km of the plant ranged from undetectable to 32.5 ppb.
Cannon SB, Veazey JM Jr, Jackson RS, Burse VW, Hayes C, Straub WE, Landrigan PJ, Liddle JA, Epidemic kepone poisoning in chemical workers, Am J Epidemiol, 1978 Jun;107(6):529-37.

- information regarding bio-availability

[26] Profiles of man-made radionuclides in sediment cores from the James River Estuary confirm the rapid burial of the pesticide Kepone. The greatest deposition of Kepone has occurred in zones of very high sedimentation rates, 10 to 20 cm/yr. Since sediment is the major Kepone reservoir, rapid burial probably reduces exposure of organisms to further contamination. Disturbance by hurricanes or dredging however, could return highly contaminated sediment to the surface although the disturbance would cause dilution with less contaminated particles
Cutshall, Norman H., Ingvar L. Larsen and Maynard M. Nichols. 1981. Man-Made Radionuclides Confirm Rapid Burial of Kepone in James River Sediments. EPA-600/J-81-220. Science. 213(4506):440-442. (ERL,GB X305).
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(f) National and international risk evaluations, assessments or profiles and labelling information and hazard classifications, as available **(provide summary information and relevant references)**

Agency for Toxic Substances and Disease Registry, USA Department of Health and Human Services. Toxicological profile for mirex and chlordecone. August 1995

(g) Status of the chemical under international conventions

OSPAR (Oslo-Paris) Convention for the Protection of the Marine Environment of the North-East Atlantic: includes chlordecone in its “List of Substances of Possible Concern on the basis of persistence, toxicity and liability to bioaccumulate (or evidence that they give rise to an equivalent level of concern)”, last revised on 21 September 2005.

Please see UNEP/POPs/POPRC.1/INF/10 Status of chemicals under consideration in other international forums.