

# Chapter 1

## Obsolete Pesticides – A Threat to Environment, Biodiversity and Human Health

Ezra J. Mrema, Federico M. Rubino, and Claudio Colosio

**Abstract** Since Rachel Carson's passionate warning in the seminal 1962 book 'Silent Spring', which is now celebrating 50 years from its publication, concern on the steadily increasing accumulation in the environment of chemically robust, biologically persistent and possibly toxic organochlorine pesticides led to their substitution with less threatening products and finally to stop or limit their production and to severely restrict their use. In particular, the Stockholm Convention on Persistent Organic Pollutants (POPs) signed in 2001 banned or greatly restricted 12 chlorinated organic compounds or classes due to their toxicity and ability to accumulate in the environment and to magnify through the global trophic network. Among them are 11 pesticides namely aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachloro-benzene, kepone, lindane, mirex, toxaphene. These pesticides played a historical role in mitigating the health impact of parasite-borne human pathogens such as malaria parasites and in protecting food crops to allow better feeding of an increasingly raising population especially in sub-tropical and tropical areas. Concern for human and environmental health is mainly due to long-term effects of some substances, in particular through endocrine disruption, interference with reproduction, carcinogenicity, although the actual size of effects of real-life exposure is still an active and debated research topic. Risk assessment and risk-benefit analysis of some key pesticides such as DDT still need a thorough understanding of the toxicity mechanisms and of its relevance to humans in the different life-stages. As a consequence of the Stockholm ban, large stockpiles of unusable pesticides accumulate in some countries and thus present considerable threat to the environment and to human

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health, also due to unavoidable degradation of the active formulated substances into poorly tractable materials. To avoid environmental damage through contamination of water and agricultural land resources by leaching or improper disposal of repositories, inventories of existing stockpiles are needed to plan and carry adequately safe disposal interventions. Methods for disposal need to tackle the peculiar chemical characteristics of these highly chlorinated aliphatic and aromatic compounds, *i.e.*, very low water solubility and an unusual stability towards acid, basic and oxidizing conditions. Research and technology development in this field is currently exploiting the most advanced 'green chemistry' approaches, aimed at an as complete mineralization of organo-chlorine substrates with as negligible production of toxic waste. We will draw a brief historical perspective of the genesis of this pivotal environmental problem, review the use of the '*dirty dozen*' pesticides and their contribution to the Green Revolution improvement of agricultural food availability, the ecotoxicological and human health concern and the current efforts to front the problems raised by their use.

**Keywords** 'Dirty dozen' • Organochlorine pesticides • Persistent Organic Pollutants • Stockholm Convention • Aldrin • Chlordane • Dieldrin • Endrin • Heptachlor • Hexachlorobenzene • Mirex • Toxaphene • DDT •  $\alpha$ -Hexachlorocyclohexane •  $\beta$ -Hexachlorocyclohexane •  $\gamma$ -hexachlorocyclohexane • Lindane • Chlordecone • Endosulfan • Pentachlorobenzene • Kepone

## 1.1 Introduction

Agricultural progresses played a pivotal role in sustaining the exponential increase of world population since the late nineteenth century and protection of crops –along with mechanization of processes, chemical fixation of nitrogen and availability of improved cultivars- has since been one of the key factors into the process. In particular, the introduction of synthetic organic chemicals in the second half of the twentieth century not only boosted the capability to counter crop- and food-spoiling organisms but also allowed to eradicate or control parasite-borne health- and life-threatening diseases such as malaria, both improving the quality of life of large populations in temperate and semi-tropical areas and allowing better utilization of agricultural areas.

The ability of early twentieth century synthetic chemists to exploit the large availability of industrial chlorine as a cheap source of chemical diversity resulted in the preparation of a wide array of compounds and materials with large utility in most fields of industrial technology. Several classes of highly-chlorinated organic molecules were found to possess strong insecticidal activity, since Muller's (re) discovery of dichloro-diphenyl-trichloroethane (DDT) in 1939, then a chemical curiosity prepared more than 60 years before as a graduate chemist's exercise in organic synthesis. Many more daughters of the intellectual creativity of industrial chemists followed within two decades and the new, powerful, cheap and relatively

safe organo-chlorine pesticides were prepared and applied on agricultural fields in the millions of tons in the following decades. The effect on agricultural landscape was striking since the beginning, both in the beneficial reduction of parasites in cultures and in the improvement of living conditions of the agricultural population, but also, in a soon much less appreciated way, as an immediately apparent decrease of landscape biodiversity. A prominent Italian poet, writer and film-maker, Pier Paolo Pasolini, even metaphorized the observation that the flash of summer fireflies had quickly disappeared from summer nights to sorrowfully point the dangerous side-effect of industrialization on people's most intimate lifestyle. By 1962 [6], since the publication of Rachel Carson's passionate book '*Silent Spring*', concern for the ecological consequences of uncontrolled application of pesticides and for their unstoppable dispersion in the general environment quickly rose, especially when highly populated regions of developed countries started to suffer the effects of widespread contamination as a threat to their own food sources. Awareness was also facilitated by the timely, although unrelated, availability of sensitive and specific methods for chemical analysis at trace level, such as gas chromatography and electron-capture detection of halogenated compounds, which allowed to empirically observe the phenomena of bioconcentration and biomagnification of these poorly degradable chemicals through their measurement in environmental compartments and in living organisms, all up the trophic levels.

As a consequence of a more than decennial effort, industrialized countries started to limit application of organochlorine pesticides, to ban their production and to enforce limits to their presence as ubiquitous contaminants of water and food. Finally an international environmental treaty, the Stockholm Convention on Persistent Organic Pollutants was signed in 2001 (effective from May 2004; amended in 2009 and 2011 with the addition of some more products), to eliminate or restrict the production and use of some priority persistent organic pollutants (POPs). Since then, while most developed countries and some of those which have trade relationship with them have in practice complied to the bid of the Convention, production, use and stockpiling were not discontinued and due to the low cost and still acceptable efficacy of some active substances, their use still continues, although on a much lesser scale.

The reduction of trace contamination from POPs at the global scale needs only to wait for their natural degradation in the environment, long as it will be the process. Two are the worthwhile scientific and technological efforts: (*a*) to better understand the natural processes of degradation of poly-chlorinated organic compounds which occur in the environment and to exploit them to accelerate the bioremediation process and (*b*) to improve our knowledge on their toxicity, especially towards the more sensitive groups of the human population, to perform a sound risk assessment aimed at forecasting their related sanitary and medical needs.

The existence of stockpiles in formerly producing or utilizing countries is a continuing threat to water and agricultural land resources, due to the possibility of contamination by illegal or inappropriate dumping of unmarketable formulated products or the unusable products which were generated over time on stocking. This in turn generates the necessity to address efforts to their safe disposal with the use of state-of-the-art knowledge and cost-effective technology.

## 1.2 The Stockholm Convention on Persistent Organic Pollutants

Early concern on the long-term consequences of the large, uncontrolled release of organochlorine pesticides into the environment led to restriction or ban to their use in an increasing number of developed Countries, along with the availability of less environmentally persistent insecticides, such as those of the organophosphate and carbamate classes. In particular, 10 years after the publication of ‘*Silent Spring*’, the USA banned DDT.

In May 1995, UNEP Governing Council initiated a global action to reduce and eliminate the release of POPs. As per UNEP definition POPs are “*chemical substances that persist in the environment, bio-accumulate through the food web, and pose a risk of causing adverse effects to human health and the environment*”. Following this, the Intergovernmental Forum on Chemical Safety (IFCS) and the International Programme on Chemical Safety (IPCS) produced the initial list of 12 POPs for assessment based on their properties and the urgency for action. These compounds were named, in journalistic jargon, as “*the dirty dozen*” and were listed in Annex A, B and C, respectively of compounds bound for elimination, restriction and limitation of unintentional production. Due to the efficacy of some polychlorinated pesticides, such as DDT and lindane, in fighting parasite-borne diseases such as malaria and scabies, respectively, exemptions allowing to continue production from registered parties and use for specific purposes are embedded into the Convention (Annex B), the enforcement of which is however a task of the individual countries.

Of the concerned chemicals, nine are poly-chlorinated pesticides (aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachloro-benzene, mirex, toxaphene), the two remaining being polychlorinated biphenyls (a class of technological substances not used as pesticides, listed twice) and polychlorinated dibenzo-dioxins and -furans (two classes of substances without known uses but unintentionally produced as contaminants in several technological processes) [26].

After a long elaboration and negotiations, the Convention was completed on 23 May 2001 in Stockholm and entered into force on 17 May 2004 with ratification by an initial 128 parties and 151 signatories (<http://chm.pops.int/>). Co-signatory States agree to outlaw nine of the dirty dozen chemicals, limit the use of DDT to malaria control, and curtail inadvertent production of dioxins and furans.

Parties to the convention agreed to periodically reviewing the list to add more compounds or classes, if they meet certain criteria for persistence and trans-boundary threat. The second set of nine new chemicals to be added to the Convention was agreed at a conference in Geneva on 8 May 2009. Of these, four are pesticides, three isomers of hexachlorocyclohexane (among which is Lindane) and chlordecone (kepone). Others are brominated flame retardants and perfluorinated organic acids, both without any connection with pesticides. In May 2011 technical endosulfan and its related isomers were added in the list. As of April, 2011, there are 173 parties to the Convention and by October 2011 three more Parties were added.

### 1.2.1 *Chemical and Toxicological Aspects of the ‘Dirty Dozen’ Organochlorine Pesticides*

Table 1.1 lists the persistent organochlorinated pesticides, along with the exemptions agreed upon for further controlled production and for restricted uses. The chemical structures, names and CAS numbers of the eleven (twelve) organochlorine pesticides (OCPs) listed in the Annexes of the Stockholm Convention are reported in Table 1.2.

OCPs can be divided according to their chemical structure into cyclodienes, dichlorodiphenyl-ethanes and hexachlorocyclohexane isomers [18]. Aldrin, Dieldrin, Endrin, Heptachlor and Chlordane belong to cyclodiene pesticides. They are synthesized by a chemical reaction technically defined as ‘cycloaddition of dienes’ (or Diels-Alder reaction, from the names of the 1950 awardees of the Chemistry Nobel Prize). Cyclodienes are prepared by reacting of the diene, hexachlorocyclopentadiene, with other unsaturated organic compounds, dienophiles, following the general scheme shown in Fig. 1.1, which illustrates the preparation of Aldrin. The key starting product, hexachloro-cyclopentadiene, in turn is prepared by chlorination of cyclopentadiene (derived in its turn from the naphtha fraction of oil).

Mirex and Kepone are also synthesized from hexachloro-cyclopentadiene but through a different chemical process (‘*cycloaddition*’), so they are not classified as ‘cyclodienes’. Lindane and Toxaphene (also known as camphechlor) are polychlorinated aliphatic hydrocarbons derived from the photochemical chlorination of benzene and camphor, respectively. DDT and hexachloro-benzene are organic substances containing chlorinated benzene rings in their structure.

As can be appreciated from their structures, their common chemical characteristics are a very poor solubility in water and a much higher solubility in organic solvents and in the lipid compartments of the living matter; most compounds also react poorly with environmental agents such as oxygen, water and light and are fairly to very resistant to biotransformation by plants, micro- and upper organisms. These properties lead to an accumulation of the compounds in the lower organisms and to the progressive increase of their presence in higher trophic levels, in marine, air and land predators, as typically exemplified by large marine mammals, deep-sea fish, circumpolar birds, penguins and polar bears. Due to poor biotransformation, saprophytic organisms which degrade animal carcasses release the pool of unaltered OCPs back into the food chain. Some compounds are subject to long range transboundary air pollution (LRTAP) due to their volatility or semivolatility properties [35]. Moreover they are able to stick (adsorb) to particulate matter in the environment. Thus they can be carried far from their application regions by means of planetary-scale air movements and ocean currents; also long-range migration of oceanic fish schools and migratory birds continuously contribute to the dispersion of the OCPs pool across the globe (long-range transportation).

From the toxicological point of view, their chemical inertness and bulky shape point at ligand-receptor interaction as the main way to display biological activity,

**Table 1.1** An extended list of persistent organochlorinated pesticides regulated by the Stockholm Convention on Persistent Organic Pollutants

| Name  | Exemptions   | Annex |
|---|--|-------|
| Aldrin <sup>a</sup>                                       | Production none<br>Use as a local ectoparasiticide and insecticide   | A     |
| Chlordane <sup>a</sup>                                    | Production by registered parties<br>Use as a local ectoparasiticide, insecticide, termiticide (including in buildings, dams and roads) and as an additive in plywood adhesives   | A     |
| Dieldrin <sup>a</sup>                                     | Production none<br>Use in agricultural operations  | A     |
| Endrin <sup>a</sup>                                       | None   | A     |
| Heptachlor <sup>a</sup>                                   | Production none<br>Use as a termiticide (including in the structure of houses and underground), for organic treatment and in underground cable boxes   | A     |
| Hexachlorobenzene <sup>a</sup>                            | Production by registered parties<br>Use as a chemical intermediate and a solvent for pesticides  | A&C   |
| Mirex <sup>a</sup>  | Production by registered parties<br>Use as a termiticide   | A     |
| Toxaphene <sup>a</sup>                                    | None   | A     |
| DDT <sup>a</sup>  | Disease vector control in accordance with Part II of Annex B<br>Production and use as an intermediate in the production of dicofol and other compounds   | B     |
| $\alpha$ -Hexachlorocyclohexane <sup>b</sup>              | None   | A     |
| $\beta$ -Hexachlorocyclohexane <sup>b</sup>               | None   | A     |
| $\gamma$ -hexachlorocyclohexane (Lindane) <sup>b</sup>    | Production none<br>Use Human health pharmaceutical for control of head lice and scabies as second line treatment   | A     |
| Chlordecone <sup>b</sup>                                  | None   | A     |
| Technical endosulfan and its related isomers <sup>c</sup> | As a broad-spectrum insecticide, endosulfan is used currently to control a wide range of pests on a variety of crops including coffee, cotton, rice, sorghum and soy   | A     |
| Pentachlorobenzene <sup>b</sup>                           | Used in PCB products, in dyestuff carriers, as fungicide, a flame retardant and as a chemical intermediate in the production of quintozone. Produced unintentionally during combustion, thermal and industrial process. Also present as impurities in solvents or pesticides | A&C   |

**Annex A** – Intentionally produced chemicals that need to be eliminated; **Annex B** – Intentionally produced chemicals with restrictions; **Annex C** – Unintentionally produced chemicals

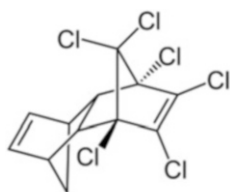
<sup>a</sup>Present in the initial list produced in 2001

<sup>b</sup>Added by the Fourth Conference of Parties, May 2009

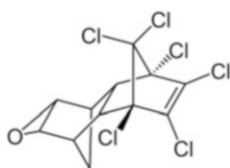
<sup>c</sup>Added by Fifth Conference of Parties, May 2011

the main exception being the radical reactivity of pentachloro- and hexachlorobenzene [19], due to its rather unique chemical characteristics of lipophilicity and possibly to conversion into the redox-active tetrachloro-1,4-benzoquinone [32]. Insecticidal activity is mostly due to interaction with ion channels in the target

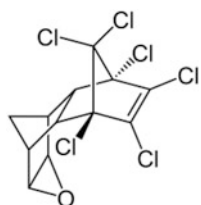
**Table 1.2** Chemical structures, names and CAS numbers of the organochlorine pesticides listed in the Annexes of the Stockholm Convention.



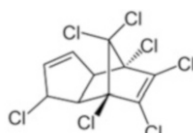
**Aldrin**; CAS: 309-00-2



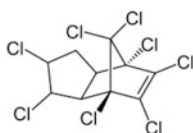
**Dieldrin**; CAS: 60-57-1



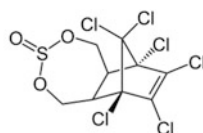
**Endrin**; CAS: 72-20-8



**Heptachlor**; CAS: 76-44-8



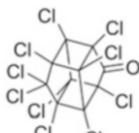
**Chlordane**; CAS: 57-74-9



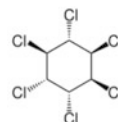
**Endosulfan**; CAS No: 115-29-7



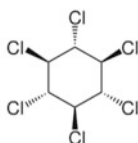
**Mirex**; CAS: 2385-85-5



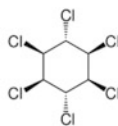
**Chlordecone (Kepone)**; CAS: 143-50-0



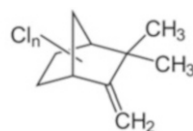
**$\alpha$ : Cyclohexane, 1,2,3,4,5,6-hexachloro-, (1 $\alpha$ ,2 $\beta$ ,3 $\alpha$ ,4 $\beta$ ,5 $\alpha$ ,6 $\beta$ )**  
CAS: 319-84-6



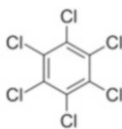
**$\beta$ -1,2,3,4,5,6-hexachlorocyclohexane**; CAS: 319-85-7



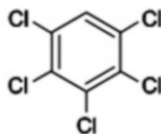
**$\gamma$ : Lindane**; CAS: 319-84-6, 319-85-7, 58-89-9



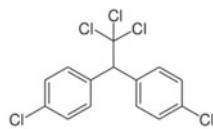
**Toxaphene**; CAS: 8001-35-2



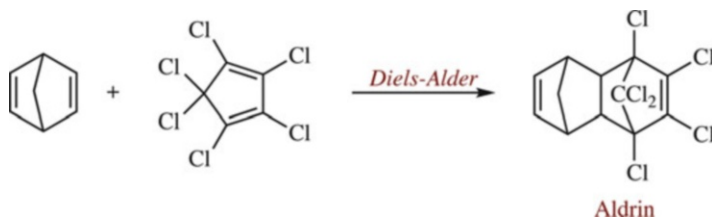
**Hexachlorobenzene**; CAS: 118-74-1



**Pentachlorobenzene**; CAS: 608-93-5



**DDT**; CAS: 50-29-3



**Fig. 1.1** General scheme for preparation of Aldrin

organisms' nervous system, a phenomenon which leads to disruption of bio-electric signalling at most organs as the pathway to organisms' death [17]. The same mechanism applies to higher animals and the human, but at considerably higher doses than the insecticidal ones. This property leads to very low toxicity towards humans, who can be harmed only in case of massive, usually accidental or deliberate exposure, and is the key reason for which OCPs were quickly accepted as key means of parasite elimination.

Concern for animals' and human health stems from interference of OCPs with biological processes leading to impairment of individuals' health or reproduction. One of the best known mechanisms is interference of DDT with calcium ion metabolism in birds, which leads to insufficient deposition in bird eggs' shells and to impaired development and early death of chicks hosted in eggs with a thinned softened shell [33]. The bald eagle (*Haliaeetus leucocephalus*), the heraldic animal of the U.S.A and the victim of widespread use of DDT, was brought to the verge of extinction by 1971 and it was only in 2007 that it was withdrawn from the list of endangered species [31].

Due to the limitation or ban to production and use, current concern for human health mainly stems from exposure of the general population to trace amounts of PCPs present as ubiquitous contaminants of the environment, in water and in food. Levels of individual exposure and of body burden depend on subjects' age, on their residence and on levels in the consumed food and water. Most toxicological information on the effects on humans at environmental levels of exposure derive from epidemiological studies. Examined groups were plant production workers, workers who applied the products for agricultural and civil and industrial, non-agricultural purposes and the general exposed populations. Although scientific and regulatory literature in the field is abundant, debate on the real extent, if any, of effects is still vocal and specific risk-benefit analyses are therefore conditioned by diverging opinions.

In the following, a necessarily brief and selective presentation of the chemical and toxicological information on each of the eleven (twelve) polychlorinated pesticides regulated by the Stockholm Convention is reported.



### 1.2.1.1 Aldrin

Aldrin is the Diels-Alder adduct of hexachlorocyclopentadiene with norbornadiene. It has been used in industry, agriculture and in public health control. Aldrin was widely used to treat seed and soil until it was banned in most countries in the 1970s. It was applied to soils to kill termites, grasshoppers, corn rootworm and other insect pests. An estimated 270 thousands of tons of aldrin and related cyclodiene pesticides were produced between 1946 and 1976. Aldrin is not toxic to insects but it is metabolically oxidized in the insect to form the epoxide **dieldrin** which is the active compound. The oxidation can also occur in soil and on plant surfaces. Aldrin residues are rarely found in foods and animals as it is rapidly converted to dieldrin. Aldrin is toxic to humans; the lethal dose of aldrin for an adult man has been estimated to be about 5 g, equivalent to 83 mg/kg b.wt. Signs and symptoms of aldrin intoxication may include headache, dizziness, nausea, general malaise, and vomiting, followed by muscle twitchings, myoclonic jerks, and convulsions. Although this may be somewhat relevant in accidental or voluntary acute intoxication, it has little, if any, relevance with regard to environmental exposure.

### 1.2.1.2 Chlordane

Chlordane is a more highly chlorinated analogue of Heptachlor, also prepared from hexachlorocyclopentadiene and cyclopentadiene, followed by chlorination. Insertion of three chlorine atoms in the molecule of the Diels-Alder adduct yields a technical mixture of two isomers,  $\alpha$  and  $\beta$ , the  $\beta$  isomer being more bioactive. The technical mixture contains chlordane, heptachlor, nonachlor and related compounds. Chlordane was first synthesized in 1944 [13] and entered the United States market from 1948 to 1988 both as a dust and an emulsified solution.

### 1.2.1.3 Chlordecone (Kepone)

Chlordecone is a degradation product of Mirex in which one *gem*-dichloride ( $>CCl_2$ ) group has been converted to a carbonyl ( $>C=O$ ) function and has been used for the same purposes. In the USA it was produced by Allied Signal Company in Hopewell, Virginia, and dumping of the substance into the James River in the 1960s and 1970s caused toxic effects on wildlife to the point that in 1975 the Governor of the State raised a ban to fishing down the James River for 100 miles, from Richmond to the Chesapeake Bay for 13 years, until efforts to clean up the river started to yield successful results. Production in the USA was stopped in 1976. In the French island of Martinique it was used without restrictions in banana plantations arguing that no alternative pesticide was available and despite a 1990 ban of the substance by France. Since 2003, the local authorities restricted cultivation of crops because the soil has been seriously contaminated by kepone. Similarly,

the nearby island of Guadeloupe was also contaminated, but to a lesser extent and has one of the highest prostate cancer rates in the world. Kepone was found to be carcinogenic in rats and mice. It induced malignant tumors in the liver of rats and mice where female rats were more susceptible to kepone exposure than male rats [24, 25]. Cannon et al. [5] observed a number of workers in Kepone production plant with clinical illness characterized by nervousness, tremor, weight loss, opsoclonus, pleuritic and joint pain, and oligospermia. The illness incidence rates for production workers (64 %) were significantly higher than for nonproduction personnel (16 %). The mean blood Kepone level was significantly higher among workers with illness than those without disease (mean: 2.53 and 0.60 ppm, respectively;  $p < 0.001$ ). Moreover, blood Kepone levels in current workers (mean, 3.12 ppm) were higher than those in former employees (1.22 ppm). However the authors did not observed apparent association between frequency of symptoms and proximity to the plant in the survey of the community population.

#### 1.2.1.4 DDT

Dichlorodiphenyltrichloroethane (DDT) was first synthesized from the reaction of chlorobenzene with chloral hydrate by a young Austrian chemist, Othmar Zeidler, a doctoral student with Adolf von Baeyer, in 1874. The substance, in fact is a mixture of *ortho*- and *para*- substituted isomers, the main one (*approx.* 77 %) being that with *para*-, *para*- substitution. Its insecticidal properties were discovered in 1939 in Paul Hermann Müller's laboratory at Ciba in Basel, Switzerland. Müller was awarded the Nobel Prize in Physiology and Medicine in 1948 "for his discovery of the high efficiency of DDT as a contact poison against several arthropods." DDT was used with great success in the second half of World War II to control malaria and typhus among civilians and troops. At the time of its discovery, the advantages of DDT that made it the best known and most useful insecticide were its stability, greater persistence, low cost, low mammalian toxicity and broad spectrum of insecticidal activity. Following more than 15 years of liberal use in agricultural and household (in the 1960s, 400,000 tons were applied annually worldwide, about 70 % for agricultural use), which resulted in the almost complete eradication of malaria in several previously endemic areas, it was Rachel Carson's passionate warning in the seminal 1962 book '*Silent Spring*' to raise concern on the ecological consequences.

#### 1.2.1.5 Dieldrin

Dieldrin is the active epoxide of aldrin and is industrially prepared by chemical epoxidation of Aldrin [4]. It is used principally to control termites and textile pests, as well as insect-borne diseases and insects living in agricultural soils. Dieldrin is toxic to humans. Based on anecdotal evidence, the lethal dose of dieldrin has been estimated to be 10 mg/kg b.wt, so it is more toxic than its metabolic precursor,

Aldrin. Signs and symptoms of acute dieldrin intoxication are essentially the same as for aldrin (*see* above). Hunter et al. [12] studied the pharmacodynamics of dieldrin in a human volunteer study. The study subjects with no recent occupational exposure to dieldrin, received 0, 10, 50, or 211  $\mu\text{g}$  dieldrin per day for 2 years. All volunteers continued in excellent health, and clinical, physiological and laboratory findings remained essentially unchanged through the 24 month exposure period and an 8-month follow up. However, workers of a chemical plant which produced several pesticides (Aldrin, Dieldrin, Endrin as well as the known animal carcinogen, dibromochloropropane) showed an increase of liver and biliary tract cancers. In 1987 IARC concluded that there is inadequate evidence for the carcinogenicity in humans, and limited evidence in experimental animals and that therefore Dieldrin is not classifiable as to its carcinogenicity in humans (Group 3).

#### 1.2.1.6 Endosulfan

Endosulfan is a close structural analogue of aldrin, chlordane, and heptachlor and is the only sulphur-containing chlorinated pesticide in the Stockholm Convention list. It is synthesized via a Diels-Alder addition of hexachloro-cyclopentadiene and cis-butene-1,4-diol in xylene, followed by cyclization of the adduct with thionyl chloride. The annual production is estimated to range between 18,000 and 20,000 tonnes worldwide. In USA, 400 tonnes are estimated to be used annually for domestic purpose. The main uses include control of pests in vegetables, fruits, cereal grains and cotton, ornamental shrubs, trees, vines and ornamental plants. It was also used to control ectoparasite on beef and lactating cattle. In Africa it is commonly used in cotton production at a dose rate between 1,000 and 2,000 g/ha while in India it is used to control pests on cashew plantations at the dose rate of 1200 g/ha. The estimated annual production in India is 9,500 tonnes, of which 4,500–5,000 tonnes are consumed domestically. Endosulfan is one of the most toxic pesticides still on the market and is responsible for many fatal pesticide poisoning incidents around the world. Since it is a GABA-gated chloride channel antagonist and a  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$  ATPase inhibitor, endosulfan is a strongly neurotoxic compound. Symptoms of acute poisoning include hyperactivity, tremors, convulsions, lack of coordination, staggering, difficulty breathing, nausea and vomiting, diarrhea, and in severe cases, unconsciousness. Doses as low as 35 mg/kg have been documented to cause death in humans, while many cases of sub-lethal poisoning have resulted in permanent brain damage. Farm workers with chronic endosulfan exposure are also at risk of rashes and skin irritation. Endosulfan is also considered a human endocrine disruptor, with the ability to delay development of the male characters in children exposed through the early age, as demonstrated by an epidemiological and monitoring study on Indian children of Kerala villages [28]. Results along the same trend were also observed in a Northern European study [7].

### 1.2.1.7 Endrin

Endrin is a stereoisomer of dieldrin, prepared by stepwise reaction of hexachlorocyclopentadiene with acetylene, followed by cyclopentadiene, followed by epoxidation [21]. About 80 % of endrin was consumed for controlling insect pests of cotton. It was also used on rice, sugar cane, grain crops, sugar beets, tobacco and cole crops. It was occasionally used in orchards as a control of rodents and as a treatment for cotton and beans seeds. It was also used as a rodenticide. Endrin has been shown to be carcinogenic at several body sites in the rat, and possibly in the mouse and in the dog [24, 25]. Several cases of acute and fatal intoxication were reported from consumption of Endrin-contaminated food in different Countries [15, 27], along with poisoning of animals and pets. One puzzling cluster of cases of seizure occurred in 1988 in the USA was reported as '*The tale of the toxic taquitos*'. Traces of Endrin were found in tortilla shells (2.4–4.6 ppm, corresponding to less than 0.1 mg per piece) purchased at an individual store by several families in Orange County (California, USA) and, based on estimates of intake from affected individuals, in this case toxic effects were observed at doses (50 micrograms/kg b. wt) four times below those previously known [34]. In comparison with dieldrin, endrin is less persistent in the environment.

### 1.2.1.8 Heptachlor

Heptachlor is prepared from hexachlorocyclopentadiene and cyclopentadiene, followed by mono-chlorination. It has both insecticidal and fumigant activity [8]. As per the Stockholm Convention, the sale of heptachlor products has been limited to the specific application of fire ant control in underground transformers. Heptachlor is rapidly oxidized to 2,3-heptachlor epoxide both photochemically in the environment, and biologically in soils and plant tissue by microsomal oxidation. Heptachlor epoxide is a more potent insecticide than heptachlor itself. Heptachlor epoxide remains in the soil for decades without significant further degradation and also dissolves more easily in water. Heptachlor and its epoxide can be absorbed to soil particles and evaporate. Compared to the more chlorinated analogue chlordane, heptachlor is about 3–5 times more active as an insecticide and more inert chemically, since it is resistant to caustic alkali. The half life of Heptachlor in the environmental compartments is ~1.3–4.2 days in air, ~0.03–0.11 years in water and ~0.11–0.34 years in soil, although one study claimed for soil a much higher half life of 2 years and that its residues were measured in soil 14 years after its initial application. Soil microorganisms transform heptachlor according to complex pattern into a range of different epoxidation, hydrolysis and reduction products. Like other POPs, heptachlor is lipophilic and poorly soluble in water (0.056 mg/L at 25 °C), thus it tends to accumulate in the body fat of humans and animals. When the compound was incubated with a mixed culture of organisms, chlordane (hexachlorocyclopentadine, its precursor) formed, which was further

metabolized to chlordene epoxide. Other metabolites include 1-hydroxychlordene, 1-hydroxy-2,3-epoxychlordene, and heptachlor epoxide. Soil microorganisms hydrolyze heptachlor to give ketochlordene. Rats metabolize heptachlor to the epoxide 1-exo-1-hydroxyheptachlor epoxide and 1,2-dihydroxydihydrochlordene. When heptachlor epoxide was incubated with microsomal preparations from liver of pigs and from houseflies, the products found were diol and 1-hydroxy-2,3-epoxychlordene [23]. Metabolic scheme in rats shows two pathways with the same metabolite. The first involves following scheme: heptachlor → heptachlor epoxide → dehydrogenated derivative of 1-exo-hydroxy-2,3-exo-epoxychlordene → 1,2-dihydroxydihydrochlordene. The second involves: Heptachlor → 1-exo-hydroxychlordene → 1-exo-hydroxy, 2,3-exo-epoxychlordene → 1,2-dihydroxydihydrochlordene [3]. Heptachlor was designated as a Class 2B or “possible human carcinogen” by The International Agency for Research on Cancer (IARC).

### 1.2.1.9 Hexachloro-Benzene

Hexachlorobenzene is a fully chlorinated derivative of benzene which was used until its 1966 ban as a fungicide for seed treatment, especially on wheat to control the fungal disease bunt. Its half life in human is estimated to be in the range of 6 years [30]. The most sensitive target organs are the liver, the ovary and the central nervous system [1]. HCB is well known to induce porphyria through a free-radical generation mechanism [19], due to its rather unique chemical characteristics of lipophilicity and possibly to conversion into the redox-active tetrachloro-1,4-benzoquinone. Eating wheat treated with hexachlorobenzene has been associated with human dermal toxicity which can result in blistering of the skin. In 1955 and 1959 consumption of bread produced with HCB-treated seeds caused epidemic of chemical porphyria in Anatolia, Turkey where 500 people were fatally poisoned and >4,000 people fell ill. The victims were affected with a liver condition called *porphyria cutanea tarda*, which disturbs the metabolism of hemoglobin and results in skin lesions. Most breastfeeding children <2 years of age, whose mothers had eaten tainted bread, died from a condition called “pembe yara” or “pink sore,” suspected to be due to high doses of HCB in the breast milk [22].

### 1.2.1.10 Hexachloro-Cyclohexane

This product is also incorrectly referred to as benzene hexachloride, but must not be confused with hexachloro-benzene, also a pesticide listed in Annex A of the Stockholm Convention. Hexachloro-cyclohexane exists in at least nine stereoisomers, of which three are of insecticidal importance and are: the  $\alpha$ -,  $\beta$ - and  $\gamma$ - isomers, the latter, which is the most active one, being also known as lindane. The crude mixture of products obtained by photochemical chlorination of benzene consists of 10–18 % of the  $\gamma$ -isomer, 55–70 % of the racemic  $\alpha$ -isomer, 5–14 %

of the  $\beta$ -isomer, 6–8 % of the  $\delta$ -isomer, 3–4 % of the  $\epsilon$ -isomer, and a trace of the  $\eta$ -isomer, along with traces of hepta- and octa-chlorocyclohexane which contribute to the unpleasant odour of technical lindane.

#### 1.2.1.11 Mirex

Mirex is the product of ‘cycloaddition’ dimerization of the hexachloro-cyclopentadiene and thus is not classified as a cyclodiene pesticide. It was popularized to control red imported fire ants (*Solenopsis saevissima richteri* and *Solenopsis invicta*) but by virtue of its chemical robustness and lipophilicity it was recognized as a bioaccumulative pollutant in aquatic and terrestrial food chains to harmful levels. As an example, after six applications of mirex bait (0.3 % mirex, corresponding to 4.2 g mirex/ha) at 1.4 kg/ha in the field, turtle fat contained 24.8 mg mirex/kg; kingfishers 1.9 mg/kg; coyote fat 6 mg/kg; opossum fat 9.5 mg/kg; raccoon fat 73.9 mg/kg. In a model ecosystem with a terrestrial-aquatic interface, sorghum seedlings were treated with mirex at 1.1 kg/ha. Caterpillars fed on these seedlings and their faeces contaminated the water which contained algae, snails, *Daphnia*, mosquito larvae, and fish. After 33 days, the ecological magnification value was 219 for fish and 1,165 for snails. Mirex is highly resistant to microbiological degradation. It only slowly dechlorinates to a monohydro derivative by anaerobic microbial action in sewage sludge and by enteric bacteria. Degradation by soil microorganisms has not been described. Ironically, the use of Mirex encouraged the spread of the red imported fire ants since it also kills native ants that are highly competitive with the fire ants. The US EPA prohibited its use in 1976 after *approx.* 250,000 kg of Mirex was applied to fields between 1962–75. IARC [14] evaluated the carcinogenic hazard resulting from exposure to Mirex and concluded that “there is sufficient evidence for its carcinogenicity to mice and rats. In the absence of adequate data in humans, based on above result it can be said that it has carcinogenic risk to humans”.

#### 1.2.1.12 Pentachlorobenzene

Pentachlorobenzene (PnCB) is not used as a pesticide itself but was the chemical precursor and production by-product and the degradation product of the fungicide pentachloro-nitrobenzene (PCNB, quintozene), a compound that is currently prepared by a different chemical route, no more involving the use of pentachlorobenzene. PCNB has itself been restricted in several Countries but still finds use in others. The chemical characteristics of PnCB allow long-range transport in air and through soil, while very poor water solubility allows bioaccumulation from water into food organisms and bio-concentration in the fat body compartments of biota. On the contrary, bio-magnification through the aquatic trophic levels is not a particularly important phenomenon. PnCB is estimated to have a half-life of 194–345 days (experimentally contaminated soil samples) and residues can persist for least 2–3 years in soil from agricultural sites [2].

Pentachlorobenzene is poorly metabolized in most species, probably because its high degree of chlorine substitution inhibits formation of the arene-oxide reactive intermediates. On the contrary, reductive dechlorination is a likely pathway for degradation and mineralization both by environmental agents (photochemical processes) and by enzymatic pathways. Its poor bio-reactivity has also consequences in explaining its carcinogenic activity [11, 20, 29], since PnCB is a “Phenobarbital-type” inducer of P450 enzymes and most likely an inducer of oxidative stress through mechanisms centred on its bio-transformation into tetrachloro-*p*-benzoquinone similar to those shown by hexachloro-benzene (*see above*).

### 1.2.1.13 Toxaphene

Toxaphene is a complex mixture obtained by chlorination of the natural terpene camphor, in which at least 670 chemicals, including chlorobornanes, chlorocamphenes, and other bicyclic chloroorganic compounds more, have been identified. At least some of them are volatile enough to be transported for long distances through the atmosphere. Toxaphene was used as an insecticide. Between 1970 and 1995, cumulative global usage of toxaphene was estimated to be 670 thousand tons. In USA during the early to mid 1970s, toxaphene became the most heavily used pesticide. Production peaked in 1975 at 30,000 tons. It was chiefly used in the cotton and soybean growing areas in the southeastern region. In California it was used to treat acariasis in cattle and this caused some deaths in cattle treated by spraying. In 1982, it was banned for most uses, and in 1990 it was banned for all uses in the United States. However, in 2010, toxaphene was still available from eleven suppliers worldwide, including seven in the U.S.A. It is classified as an IARC Group 2B carcinogen.

## 1.3 Obsolete Pesticides as a Problem of Global Concern

Obsolete pesticides are stocked pesticides that can no longer be used for their intended purpose or any other purpose and therefore require disposal [9]. Obsolete pesticide stockpiles are an international environmental policy issue thus its management needs to be given a global attention to save our resources. In the developing countries and in many Central and Eastern European countries, there are huge stockpiles of pesticides, estimated to be several hundreds of thousands of tones [16]. Estimates show that >500,000 tons of obsolete pesticides are accumulated globally, especially in developing countries [10]. A considerable amount of the accumulated obsolete pesticides are in the group of persistent organic pollutants (POPs). The cause of accumulation of these chemicals has been attributed to lack of appropriate management, misuse of chemicals, uncoordinated chemical donations, substandard storage, poor storekeeping, lack of expertise and financial resources. Other factors include banning or restriction of products for health or environmental

reasons e.g. through banning as for the case of those which were banned or restricted by Stockholm Convention; withdrawal of registration; or policy decision by the Ministry of Agriculture or other authorized ministries. As a result of improper or prolonged storage some products can no longer be used according to its label specifications and instructions for use, nor can it easily be reformulated to become usable again and thus lead to deterioration of these products. A product is considered deteriorated when:

- it has undergone chemical and/or physical changes that result in phytotoxic effects on the target crop;
- causes an unacceptable hazard to human health or the environment;
- the product has undergone an unacceptable loss of biological efficacy because of degradation of its active ingredient and/or other chemical or physical changes;
- its physical properties have changed to such an extent that it can no longer be applied with standard or stipulated application equipment.

To determine whether a pesticide is obsolete and need for disposal a decision tree has been constructed to assist this decision making process (see Fig. 1.1 from [9]).

The accumulation and bad management of obsolete pesticides constitute a threat to human health and the environment, locally, regionally and globally. When located near water sources, obsolete pesticides can pose a high risk of contaminating drinking water sources as well as irrigation water. In turn contaminated irrigation water might introduce pesticide residues into crops and fish, making them unfit for trade as well as for local consumption. Leaking of stockpile can contaminate a significant land area making it unfit for human habitation or for any agricultural activities [36].

## 1.4 Safe Disposal of Stockpiles and Bioremediation of Contaminated Areas

Industrial production of polychlorinated organic compounds such as pesticides is far from being an innocuous activity, in that it generates large quantities of toxic waste per unit of marketable active ingredient, even if the formulated products contain technical mixtures of active substances. As an example, the manufacture of lindane, which is still authorized by the Stockholm Convention as a scabicide entails the chlorination of benzene in the presence of UV light ('photo-chlorination') to form a mixture of isomers, among which  $\alpha$ - (70 %),  $\beta$ - (12 %),  $\gamma$ - (10 %, the desired active substance) and  $\delta$ - (7 %) HCH, respectively. Lindane is purified from rest of the HCH isomers and the rest becomes an environmental liability. Therefore manufacture of 1 tonne of lindane produces at least 9 tonnes of waste just from synthesis yield, not even considering solvents used for extraction from the raw product and crystallization of the desired isomer to a suitable purity of 99.9 %.



Once off-products of the fine chemicals industry accumulate in production and formulation plants, they are at best stored in containers steel or plastic drums and stockpiled in ground holes, usually within or close to production yards. Solids may be directly dumped into the ground. Long-term disposal used to be of lesser concern until very recent times, especially in Countries where regulations and controls were lacking and safe technologies poorly available.

The problem of disposal of hazardous chemical wastes is common not only to chemical plants, but also to other sectors of concern for public health and safety such as disposal of spent ammunition, of banned weapons such as chemical warfare agents, of expired pharmaceuticals. Most of the involved chemicals can harm the environment and adversely influence human health by contaminating water streams and tables, agricultural land and dwelling sites.

Remediation is a costly and often unsolvable process and may leave to several future generations ahead an economic and human burden which is difficult to cope with. However, currently available technology is at least in part able to address such problems or to stabilize current situations in the view that in near future better technologies will be available for permanent solutions.

**Dumping** into long-term disposal sites has long been the preferred way to get rid of solid industrial waste. At least in the past, little if any care was given to prevent leaching of the contents from corroded or pierced vessels by isolating the walls of the dig or even to take note of the position of filled up digs. This caused the unexpected and uncontrolled release or leaching of hazardous chemical waste into lower-lying water tables and downstream carryover of toxic products. Nowadays intermediate- to long-term dumping sites can be established by means of comprehensive technologies which include geological, geochemical and hydrogeological assessment of the selected sites with reference to ground permeability and to presence of reachable water sources. Clay layers are mostly impermeable to water and counter diffusion of leachates. The walls of digs are usually lined with multiple layers of waterproof synthetic materials such as polyvinyl-chloride. Since sand and gravel readily absorb water, layers can be employed to drive the flow of leached materials to inspection drills, which are commonly employed to monitor the permeation of leachates and to draw the permeated liquids towards safe treatment and disposal.

**High-temperature incineration** is still the technique of choice for the permanent solution to disposal of toxic chemical wastes. At sufficiently high temperature any organic substance reacts with air or oxygen to yield the thermodynamically favoured products carbon dioxide and water, while sulphur, phosphorus and the halogen are converted into the corresponding acidic products. The very problem of incineration is that a high proportion of hetero-atoms, especially the halogens impair the natural processes of combustion by quenching the free radical propagation processes which lead to the extensive decomposition of complex molecules into the final combustion products. As a consequence, new, kinetically stable molecules generate from the radical species in the combustion environment, such as polycyclic aromatic hydrocarbons and carbon soot, chlorinated dibenzo-dioxins and –furans, which are of a major concern for human health and for that reason are

also considered by the Stockholm Convention. To minimize emission into the environment especially of chlorinated dibenzo-dioxins and -furans from incineration of chlorinated organic waste, which include not only pesticides (which are mostly banned) but mainly organic polymers used for packaging or as structural material for industrial goods specific techniques have been developed. In principle, factors which lead to *de-novo* formation of these products are quite large in number, yet to be subdivided into two groups with various mutual interactions: (a) those related to operational factors (poor combustion conditions, locally insufficient oxygen and mixing of oxygen-rich and oxygen-lean combustion products, or inadequate temperature, residence time, and turbulence, the so-called 3 T's) and (b) those related to chemical and catalytic factors (elemental composition of waste and local composition of combustion products, catalysis from chemical species, especially metals such as copper, present in ashes). Among the strategies adopted to lower the net emission of dioxin-like compounds from incinerators, the use of alkaline conditions, such as by using chlorinated waste as an additive to fuel in the manufacture of Portland cement in kilns (co-combustion). However, the destruction of stockpiles of obsolete chlorinated pesticides is mostly considered a remediation intervention, rather than a routine process in waste management (as in the case of chlorinated plastics) also due to the very high proportion of chlorine in the mixtures, which is well over 60 % on a by-weight basis. As a consequence, dedicated facilities aimed at complete destruction with minimal production of toxic end-products are employed.

**Supercritical Water Oxidation (SCWO)** is an emerging and promising technique for the mineralization of organic substances which are not easily amenable to incineration or biodegradation. This technique exploits the unique properties of water at supercritical conditions, *i.e.*, at high temperature (above 370.15 °C) and pressure (above 221.2 bar), when the vapor and liquid are indistinguishable and several properties of water suddenly change. Supercritical water exhibits high gas-like diffusion rates along with high liquid-like collision rates, the behavior of water as a solvent is reversed in comparison to that of subcritical liquid water and, as a result, the solubility of organic non-polar compounds such as chlorinated hydrocarbons greatly increases while polar substances such as inorganic salts precipitate out of solution. As a consequence, reaction of dissolved organic compounds with oxidants, and even with dissolved oxygen occurs under essentially single-phase conditions, and complete mineralization of organic substance to carbon dioxide, water and inorganic salts can be achieved with great efficiency and in shortened time. Heteroatoms, such as chlorine, that are bound to the organic will produce hydrochloric acid; organic-bound sulfur and phosphorous are oxidized to sulfuric acid and phosphoric acid respectively and metals are oxidized to their highest oxidation state (*e.g.*, iron to iron rust, chromium to chromium oxide). SCWO for destroying hazardous wastes involves supercritical water as the reaction medium, and an oxidant such as air, oxygen or nitrogen oxide at a relatively high temperature and pressure (235 bar and 650 °C), yet much lower than that required in gas-phase incineration. Among the drawbacks which still hamper the large scale application of SCWO is corrosion of reactors by

the very reactive conditions, which dictates the use of resistant materials. In practice, no operative facilities beyond investigational stage are known to be active in this field.

**Bioremediation** is a process in which indigenous or inoculated micro-organisms such as fungi, bacteria and other microbes degrade (metabolize) organic contaminants. Nutrients, oxygen or other amendments may be used to enhance bioremediation and contaminant desorption from subsurface materials. This procedure have been successfully used to remediate soils, sludges and ground water contaminated with petroleum hydrocarbons, solvents, pesticides, wood preservatives, and other organic chemicals. Bioremediation is especially effective for remediating low level residual contamination in conjunction with source removal. It does not require heating; rather it requires relatively inexpensive inputs, such as nutrients. Thus it is a more cost effective as compared to incineration and physical and chemical methods.

Enhanced bioremediation does not generate residuals requiring additional treatment or disposal. When conducted in situ, it does not require excavation of contaminated media. Treatability or feasibility tests are performed to determine whether enhanced bioremediation is feasible in a given situation, and to define the remediation time frame and parameters. The length of time required for treatment can range from 6 months to 5 years and is dependent on many site-specific factors.

Cleanup goals may not be attained if the soil matrix prohibits contaminant microorganism contact. The circulation of water-based solutions through the soil may increase contaminant mobility and necessitate treatment of underlying ground water. Preferential colonisation by microbes may occur causing clogging of nutrient and water injection wells. Preferential flow paths may severely decrease contact between injected fluids and contaminants throughout the contaminated zones. The system should not be used for clay, highly layered, or heterogeneous subsurface environments because of oxygen (or other electron acceptor) transfer limitations. High concentrations of heavy metals, highly chlorinated organics, long chain hydrocarbons, or inorganic salts are likely to be toxic to some microorganisms. Those compounds that resist biodegradation are often not capable of efficient treatment using bioremediation and an alternative must be found. Bioremediation slows at low temperatures. Many of the above factors can be controlled with proper attention to good engineering practice.

## 1.5 Conclusions

Polychlorinated pesticides played an important role in the Green Revolution to increase agricultural production and in eradicating or controlling parasite-borne diseases such as malaria in temperate and sub-tropical areas of the world. However, their impact on environmental biodiversity was not negligible due to their

environmental persistence, poor biodegradation and biomagnifications into and along the planetary trophic network. Also their effect on the long-term health of the different sub-groups of the human population needs a thorough assessment based on sound toxicological knowledge, on accurate dosimetry in the different scenarios and on responsible evaluation of risk/benefit relationship.

The burden of final disposal of stockpiles and of remediation of contaminated sites is a benchmark of international cooperation both on openness in the circulation of information and in sharing state-of-the-art technology.

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