

and supportive with treatment of CNS stimulation such as hyperactivity and convulsions.

#### ◇ References.

1. WHO. Safe use of pesticides: fourteenth report of the WHO expert committee on vector biology and control. *WHO Tech Rep Ser 813* 1991. Available at: [http://libdoc.who.int/trs/WHO\\_TRS\\_813.pdf](http://libdoc.who.int/trs/WHO_TRS_813.pdf) (accessed 24/07/08)
2. Proudfoot A, ed. Pesticide poisoning: notes for the guidance of medical practitioners. 2nd ed. London: DoH, The Stationery Office, 1996.

#### Uses

The chlorinated or organochlorine insecticides were widely used but, because of persistence in man, many have been banned or restricted.

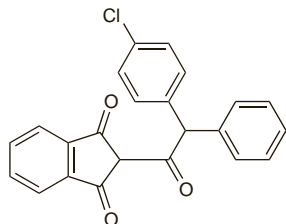
#### ◇ References.

1. WHO. Polychlorinated biphenyls and terphenyls. *Environmental Health Criteria 140*. Geneva: WHO, 1992. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc140.htm> (accessed 28/05/04)
2. WHO. Polychlorinated biphenyls and polychlorinated terphenyls (PCBs and PCTs) health and safety guide. *IPCS Health and Safety Guide 68*. Geneva: WHO, 1992. Available at: <http://www.inchem.org/documents/hsg/hsg/hsg68.htm> (accessed 28/05/04)

### Chlorophacinone

Clorofacinona; LM-91. 2-[2-(4-Chlorophenyl)-2-phenylacetyl]indane-1,3-dione.

$C_{23}H_{15}ClO_3 = 374.8$ .  
CAS — 3691-35-8.



#### Profile

Chlorophacinone is an indanedione derivative used as an anticoagulant rodenticide. It is also reported to uncouple oxidative phosphorylation with consequent stimulation of cellular metabolism which may contribute to its toxicity.

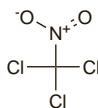
#### ◇ References.

1. Burucoa C, et al. Chlorophacinone intoxication: biological and toxicological study. *J Toxicol Clin Toxicol* 1989; **27**: 79–89.
2. WHO. Anticoagulant rodenticides. *Environmental Health Criteria 175*. Geneva: WHO, 1995. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc175.htm> (accessed 28/05/04)
3. Lagrange F, et al. Toxicological management of chlorophacinone poisoning. *Acta Clin Belg Suppl* 1999; **1**: 13–16.
4. Papin F, et al. Lethal paradoxical cerebral vein thrombosis due to suspicious anticoagulant rodenticide intoxication with chlorophacinone. *Forensic Sci Int* 2007; **166**: 85–90.

### Chloropicrin

Cloropicrina; Nitrochloroform. Trichloronitromethane.

$CCl_3NO_2 = 164.4$ .  
CAS — 76-06-2.



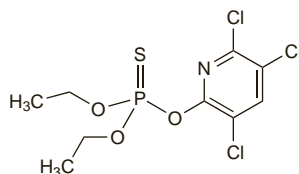
#### Profile

Chloropicrin is a lachrymatory agent with an intense odour. It is intensely irritating to the skin and mucous membranes. It is an insecticide and is used for fumigating stored grain and soil. Chloropicrin is also added to other fumigants as a warning gas.

### Chlorpyrifos (BAN)

Clorpirifós. O,O-Diethyl O-3,5,6-trichloro-2-pyridyl phosphorothioate.

$C_9H_{11}Cl_3NO_3PS = 350.6$ .  
CAS — 2921-88-2.



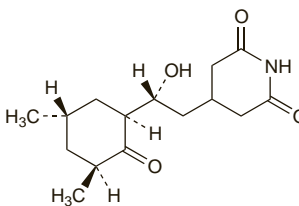
#### Profile

Chlorpyrifos is an organophosphorus insecticide (p.2047) used in agriculture.

### Cicloheximide (rINN)

Cicloheximida; Cicloheximidum; Cycloheximide (USAN); U-4527. 3-[(2R)-2-[(1S,3S,5S)-3,5-Dimethyl-2-oxocyclohexyl]-2-hydroxyethyl]glutaramide.

Циклогексимида  
 $C_{15}H_{23}NO_4 = 281.3$ .  
CAS — 66-81-9.



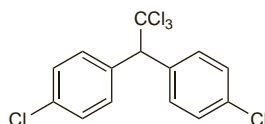
#### Profile

Cicloheximide is an antimicrobial substance produced by strains of *Streptomyces griseus*. It has antifungal properties and has been used for the treatment and control of certain mycotic plant diseases.

### Clofenotane (rINN)

Chlorofenotano; Chlorophenothane; Chlorphenothanum; Clófenotane; Clofenotano; Clofenotanum; DDT; Dichlorodiphenyltrichloroethane; Dichophanum; Dicophane; Klofenotaani; Klofenotan. 1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane.

КЛОФЕНОТАН  
 $C_{14}H_9Cl_5 = 354.5$ .  
CAS — 50-29-3.  
ATC — P03AB01.  
ATC Vet — QP53AB01.



#### Pharmacopoeias. In It.

#### Adverse Effects and Treatment

As for Chlorinated Insecticides, p.2037.

#### ◇ References.

1. WHO. DDT and its derivatives. *Environmental Health Criteria 9*. Geneva: WHO, 1979. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc009.htm> (accessed 28/05/04)
2. WHO. DDT and its derivatives—environmental aspects. *Environmental Health Criteria 83*. Geneva: WHO, 1989. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc83.htm> (accessed 28/05/04)

**Carcinogenicity.** Some small epidemiological studies have suggested that certain organochlorines, namely 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), a metabolite of clofenotane, and polychlorinated biphenyls (PCBs), might increase the risk of breast cancer in women. However, re-analysis<sup>1,2</sup> of the available data indicated that an association with breast cancer was unlikely for clofenotane; there was no evidence for an association with the PCBs. Any link between exposure to clofenotane and the development of testicular cancer in men was also refuted<sup>3</sup> after long-term monitoring of populations in Scandinavia.

1. Key T, Reeves G. Organochlorines in the environment and breast cancer. *BMJ* 1994; **308**: 1520–1.
2. van't Veer P, et al. DDT (dicophane) and postmenopausal breast cancer in Europe: case-control study. *BMJ* 1997; **315**: 81–5.
3. Ekholm A, et al. DDT and testicular cancer. *Lancet* 1996; **347**: 553–4.

**Effects on fertility.** A metabolite of clofenotane, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), was reported<sup>1</sup> to have anti-androgenic properties in rats and exposure to clofenotane might account for a previously reported decline in male fertility and an increase in male reproductive abnormalities.

1. Keke WR, et al. Persistent DDT metabolite p,p'-DDE is a potent androgen receptor antagonist. *Nature* 1995; **375**: 581–5.

**Effects on the nervous system.** A retrospective study<sup>1</sup> found that retired malaria workers exposed long-term to clofenotane did less well in neurobehavioural tests than a control group, and had an increase in neuropsychological and psychiatric symptoms.

1. van Wendel de Joode B, et al. Chronic nervous-system effects of long-term occupational exposure to DDT. *Lancet* 2001; **357**: 1014–16.

**Pregnancy.** In a large prospective study<sup>1</sup> of children born between 1959 and 1966, an association was found between preterm births and small-for-gestational-age babies, and maternal concentrations of a metabolite of clofenotane, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) measured in serum samples which had been stored during pregnancy.

1. Longnecker MP, et al. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. *Lancet* 2001; **358**: 110–14.

#### Pharmacokinetics

Clofenotane may be absorbed after ingestion or inhalation or through the skin. Clofenotane is stored in the body, particularly in body fat, and is very slowly eliminated. It crosses the placenta and appears in breast milk. It is metabolised in the body to the ethylene derivative, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE); the acetic acid derivative (DDA) also appears in the urine.

#### Uses

Clofenotane is a chlorinated insecticide (p.2037). It is a stomach and contact poison and retains its activity for long periods under a variety of conditions. It is effective against disease vectors such as fleas, lice, and mosquitoes and has been applied topically for pediculosis (p.2034) and scabies (p.2035), although more suitable alternatives exist.

Because of the extreme persistence of clofenotane, concern over its effect in the environment, and the problem of resistance, the widespread use of clofenotane is now generally discouraged. It is no longer used in some countries while in others its use is limited.

◇ Despite reservations regarding the use of clofenotane for vector control, many countries have relied on it for the control of both malaria and visceral leishmaniasis. WHO has concluded<sup>1,2</sup> that clofenotane might be used provided:

- that it was used only for indoor spraying
- that it was known to be effective
- that it was manufactured to WHO's specifications
- that the necessary safety precautions were taken in its use and disposal

However, they recommended further investigation of the effects of clofenotane in breast milk and of suspected carcinogenicity, as well as clarification of the significance of the reduced density of muscarinic receptors caused by clofenotane.

1. WHO. WHO expert committee on malaria: twentieth report. *WHO Tech Rep Ser 892* 2000. Available at: [http://libdoc.who.int/trs/WHO\\_TRS\\_892.pdf](http://libdoc.who.int/trs/WHO_TRS_892.pdf) (accessed 21/07/08)
2. WHO Global Malaria Programme. Indoor residual spraying: use of indoor residual spraying for scaling up global malaria control and elimination 2006. Available at: <http://malaria.who.int/docs/IRS-position.pdf> (accessed 21/04/08)

#### Preparations

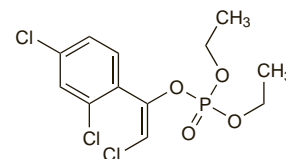
**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** *Ital:* Antiscabbia Candioli at DDT Therapeutico.

### Clofenvinfos (BAN, rINN)

Chlorfenvinfos; Chlorofenvinfos; Clofenvinfós; Clofeninfosum. 2-Chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate.

Клофенвинфос  
 $C_{12}H_{14}Cl_3O_4P = 359.6$ .  
CAS — 470-90-6.



#### Profile

Clofenvinfos is an organophosphorus insecticide (p.2047) used in agriculture.