**POPRC-10/3: Dicofol**

*The Persistent Organic Pollutants Review Committee,*

*Having examined* the proposal by the European Union to list dicofol in Annexes A, B and/or C to the Stockholm Convention and having applied the screening criteria specified in Annex D to the Convention,

1. *Decides,* in accordance with paragraph 4 (a) of Article 8 of the Convention, that it is satisfied that the screening criteria have been fulfilled for dicofol as described in the evaluation contained in the annex to the present decision;

2. *Also* *decides,* in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of the annex to decision SC-1/7, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention;

3. *Invites,* in accordance with paragraph 4 (a) of Article 8 of the Convention, parties and observers to submit to the Secretariat the information specified in Annex E before 5 January 2015.

**Annex to decision POPRC-10/3**

**Evaluation of dicofol against the criteria of Annex D**

**A. Background**

1. The primary source of information for the preparation of the present evaluation was the proposal submitted by the European Union (UNEP/POPS/POPRC.9/3), which is a party to the Convention.

2. Additional sources of scientific information included critical reviews prepared by recognized authorities.

**B. Evaluation**

3. The proposal was evaluated in the light of the requirements of Annex D to the Convention regarding the identification of the chemical (paragraph 1 (a)) and the screening criteria (paragraphs 1 (b)–(e)):

**(a) Chemical identity:**

(i) Adequate information was provided in the proposal, which relates to dicofol, CAS No. 115-32-2 and its isomers   
(*p,p'*-dicofol, CAS No: 115-32-2; and *o,p'*-dicofol, CAS No. 10606-46-9);

(ii) The chemical structures were provided;

The chemical identity of dicofol and its isomers is adequately established;

**(b) Persistence:**

(i) Degradation in water is primarily by hydrolysis. At a pH of 5, the half-life of dicofol’s main *p,p’*-isomer was 85 days, fulfilling the cut-off value of 60 days for persistence in water. Approximately 10 per cent of northern European Union member State surface waters have a pH of around 5 (Refs. 1, 2). Also, blackwater rivers found in several areas around the world (Australia, Amazonia, Europe, Indonesia, the Orinoco basin and the northern and southern areas of the United States) typically have a pH of around 5. Conservative estimates for half-life in aerobic soil of dicofol (considering the parent compound and its major degradates) are as high as 313 days, fulfilling the cut-off value of 6 months for persistence in water. Isomers of dicofol are hydrolized relatively quickly at neutral and alkaline pH. Both isomers are hydrolized within 8 hours at a pH of 7, with half-lives of 64 hours. Dicofol is hydrolized very rapidly under neutral and alkaline conditions (Ref. 3);

(ii) According to the database of the National Institute of Technology and Evaluation (NITE) of Japan, dicofol is characterized as non‑biodegradable;

There is sufficient evidence that dicofol meets the persistence criterion;

**(c) Bioaccumulation:**

(i) A study with *p,p’*-dicofol in bluegill sunfish resulted in a bioconcentration factor (BCF) of 10,000. A study of fathead minnows reported BCF values as high as 43,000 after 296 days of exposure to dicofol. Residues of *p,p’*-dicofol accumulated in bluegill sunfish with BCF of 6,600, 17,000 and 10,000 in fillet, viscera and whole fish, respectively, during 28 days of exposure. No information is available on bioaccumulation in fish for *o,p’*-dicofol since *o,p’*-dicofol hydrolizes quickly (Ref. 3). BCF values of 8,200 and 6,100 obtained for common carp were available in the NITE database, which were in the same range as the BCF values found in another study involving zebra fish. Comparison with BCF values obtained from QSAR models showed good agreement with those obtained in the study with zebra fish. There is therefore strong evidence from several fish studies indicating that BCF values are above the threshold of 5,000;

Metabolism testing on rat elimination half-lives were estimated to be   
1.5–4 days for *o,p’*-dicofol and 4–7 days for *p,p’-*dicofol (Ref. 4);

The measured log Kow value of dicofol is 4.30 according to the Pesticide Manual (14thedition 2012). Measured log Kow values vary from 4.08 to 5.02. A high log Kow of 6.06 has been reported (Ref. 3). A high log Koa of 8.9 is reported in air-breathing organisms (Ref. 5);

There is sufficient evidence that dicofol meets the bioaccumulation criterion;

**(d) Potential for long-range environmental transport:**

(i) and (ii) There are little data on the presence of dicofol in remote areas. Dicofol has been detected in the Arctic environment (Ref. 6);

(iii) The estimated atmospheric half-life exceeds the screening criteria of 2 days   
(3–10.5 days). The calculated transport distance in Europe is 1,650 km for dicofol (Ref.1);

There is sufficient evidence that dicofol meets the criterion on potential for long-range environmental transport;

**(e) Adverse effects:**

(i) There are no specific data available;

(ii) There are animal data showing a potential of dicofol to have adverse effects on human health, including effects on the liver, kidney, adrenal gland and urinary bladder. The no observed adverse effect level (NOAEL) for induction in mice is 2.1 mg/kg bw/day. In document UNEP/POPS/POPRC.8/INF/13, the Committee concluded that based on available data there was no evidence of the carcinogenicity of dicofol. However, a recent study (Ref. 7) indicates that dicofol might raise the risk of cancer incidence through effects on the frame conformation of proteins, disturbing their physiological function;

In a two-year study of rats, growth, enzyme induction and other changes in the liver, adrenal gland and urinary bladder were observed at doses of 2.5 mg/kg/day, resulting in a limit dose value, acceptable daily intake (ADI), of 0.0022 mg/kg bw/day (Ref. 8);

In another two-year study on hormonal effects in dogs a NOAEL of 0.22 mg/kg/day has been determined, leading to a reference dose (RfD) of 0.0004 mg/kg/day (Ref. 3);

A dietary concentration of 7 mg/kg of dicofol fed to mice for three generations produced defects in 12-day-old offspring of the third generation. Effects, however, were not identified in another study with rabbits at similar or higher exposure levels;

Dicofol is highly toxic to aquatic animals as defined in the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). It is classified as aquatic acute and chronic category 1 in the European Union’s regulation on the classification, labelling and packing of substances and mixtures (Regulation (EC) No. 1272/2008);

The lowest LC50 for fish is 0.053 mg/l; the lowest value for crustaceans is 0.06 mg/l (Ref.9);

The no observed effect concentration (NOEC) in a 60-d fish early life stage test was 4.4 μg/l and NOEC for chronic exposure was 4.5 – 9 μg/l. The United States Environmental Protection Agency reregistration eligibility decision for dicofol (1998) (Ref. 3) cites effects on the reproductive physiology of the fathead minnow from concentrations as low as 5 μg/l;

A two-generation study of reproductive and morphological effects of dicofol on captive American kestrelsby MacLellan *et al.* (1996) showed significantly thinner egg shells at 20 mg/kg of dicofol. Male embryos from females dosed with 5 and 20 mg/kg of dicofol had gonads that were significantly different from those of control chicks (Ref. 10);

Wiemeyer *et al.* (2001) reported that the lowest observed dietary effect concentration for eggshell thinning was 3 mg/kg and that the no observed adverse effect concentration (NOAEC) was 1 μg/g (Ref. 11). This is slightly lower than the NOEC of 2.5 mg/kg for eggshell thinning in ducks reported by Belfroid A. *et al.* (2005) (Ref.1);

According to the OSPAR document on dicofol (Ref. 9), the pattern and magnitude of dicofol on eggshell thinning was similar as that observed with   
*p,p’*-DDE. Schwarzbach *et al.* (1988), cited in OSPAR (2002) (Ref.9), showed that dicofol was not metabolized to DDE in birds and therefore concluded that the adverse effect was caused by dicofol itself;

In a study with earthworms by Shi *et al.* (2006), dicofol significantly inhibited the reproductive ability of earthworms (Ref. 12);

Lavado *et al.* (2004) (Ref. 13) and Thibaut and Porte (2004) (Ref. 14) showed that dicofol could interfere with the synthesis of sex hormones in fish microsomes;

Haeba *et al.* (2008) (Ref. 15) demonstrated in daphnia that 0.1 mg/l of dicofol resulted in a significant shift of the sex ratio in favour of males at 0.1 mg/l. Kojima *et al.* (2004) (Ref. 16) showed estrogenic activity of dicofol in an in vitro test;

Endocrine effects were also observed by Vinggaard *et al.* (2000) (Ref. 17), Okubo *et al.*(2004) (Ref. 18), Hoekstra *et al.* (2006) (Ref. 19) and Thiel *et al.* (2011) (Ref. 20).

There is sufficient evidence that dicofol meets the criterion on adverse effects;

**C. Conclusion**

4. The Committee concluded that dicofol met the screening criteria specified in Annex D.

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