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Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
Chemical Review Committee
Second meeting
Geneva, 13–17 February 2006
Item 5 (b) of the provisional agenda*

Inclusion of chemicals in Annex III of the Rotterdam Convention: review of notifications of final regulatory actions to ban or severely restrict a chemical: cyhexatin

Cyhexatin: supporting documentation provided by Japan

Note by the secretariat

The annex to the present note contains the supporting documentation provided by Japan in support of its final regulatory action on cyhexatin.

* UNEP/FAO/RC/CRC.2/1.

K0584427 131205

Annex

List of supporting documentation on Cyhexatin from Japan

- Focussed Summary

The Japanese DNA for the PIC Convention would like to submit the following information on our notification of final regulatory action on Cyhexatin.

I. Supporting Documentation

1. Risk or hazard evaluation referenced in Section 2.3 of the notification form
   See Annex.

2. Relevant documentation for Section 2.4.1, referring to protecting human health
   Teratology studies in rats and rabbits indicated that cyhexatin was teratogenic and it was found that it could not establish NOAEL from the result. Therefore, it was assessed that the ADI be withdrawn taking account of the result on Food Sanitation Investigation Council of Ministry of Health and Welfare in 1994.

3. Any other information used in making the decision to ban this chemical
   No information.

II. Trade Information

1. Manufacture within Japan and the export destination if manufactured
   The total amount of the domestic manufacture as pesticide for agricultural use is 1,996 t from 1984 to 1987. No export experience has been reported.

2. The date the chemicals were last imported into Japan
   No import experience has been reported.

Focused Summary

1. Introduction

a) The events that led to the regulatory action
   The agricultural chemicals registration of all products including Cyhexatin was voluntary canceled by the manufacturer.
   In 2002, non-registered products including Cyhexatin was distributed and used nationwide. Therefore, the distribution and use were prohibited under the ministerial ordinance taking into consideration human health.

b) Significance of regulatory action, eg one use or many uses, level or degree of exposure
   Since March 10, 2003, sale and use of Cyhexatin have been banned.

c) An overview of the regulatory system of the notifying country if relevant
   The Ministry of Agriculture, Forestry and Fisheries is responsible for the regulation of pesticide for agricultural use on manufacture, distribution, import and us e in Japan. Under the Agricultural Chemicals Regulation Law, the manufacture, distribution, import and use of the pesticide is banned without the registration by the Minister of Agriculture, Forestry and Fisheries.
   The registration has been conducted with the standards for the toxicity and the residue in water, soil and crops.

d) Scope of the regulatory action – precise description of the chemicals subject to the regulatory action
Aforementioned in b), the distribution and use of Cyhexatin has been prohibited.

2. Risk Evaluation

a) Key findings of the national risk evaluation
See Annex.

b) Key data reviews consulted and a brief description
See Annex.

c) Reference to national studies, eg toxicological and ecotoxicity studies
See Annex.

d) Summary of actual (potential) human exposure and/or environmental fate
See Annex.

3. Risk Reduction and Relevance to Other States

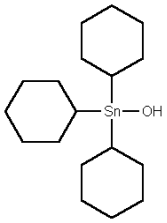
a) Estimates of the quantity of chemicals used, or imported/exported at the time of the regulatory action and if possible information on ongoing trade
No use, export or import of Cyhexatin.

b) Relevance to other States i.e. those with similar conditions of use
No information.

c) Comments on the typical use of the chemical within the notifying country, with comments on possible misuse (if appropriate)
Insecticide on the typical use.

Annex

<table>
<tr><td>CAS-No.</td><td>13121-70-5</td></tr>
<tr><td>Name

Formula</td><td>Tricyclohexyltin hydroxide (common name : Cyhexatin)
 

$C_{18}H_{34}OSn$</td></tr>
<tr><td>Description</td><td>White powder [1)]</td></tr>
<tr><td>Melting point</td><td>195~198 ˚C (decomp.) [1)]</td></tr>
<tr><td>Boiling point</td><td>-</td></tr>
<tr><td>Vapor pressure</td><td>Negligible [ )]</td></tr>
<tr><td>Solubility</td><td>Water: <1mg/l, Acetone: 1.3g/kg, Methanol: 37g/kg, Dichloromethane: 34g/kg, Chloroform: 216g/kg, Carbon tetrachloride: 28g/kg, Toluene: 10g/kg [1)]</td></tr>
<tr><td>Persistence</td><td>Available data are insufficient to fully assess the environmental fate. [2)]</td></tr>
<tr><td>Bio-accumulation</td><td>Data is not available
<table>
<tr><td></td><td>Species</td><td>Age</td><td>Exposure period</td><td>BCF</td></tr>
<tr><td>Fish</td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Crustacea</td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td rowspan="3">Mutagenicity</td><td>Ames</td><td>Data is not available</td></tr>
<tr><td>chromosomal aberration</td><td>Data is not available</td></tr>
<tr><td>in vivo dominant lethal test</td><td>Data is not available</td></tr>
<tr><td rowspan="4">90 days repeat dose toxicity</td><td>Species</td><td>Mouse</td></tr>
<tr><td>Vehicle</td><td>Diet</td></tr>
<tr><td>Dose</td><td>25, 50, 100, 200, 400, 800, 1600ppm [3)]</td></tr>
<tr><td>NOAEL</td><td>25ppm (3.8mg/kg/day)</td></tr>
</table>

	Effects	Weight gain was depressed in females of 50ppm group and. Both sexs at higher level. Shrinkage or disappearance of follicles was seen in 800ppm group and 8/10 on 400ppm diet.
90 days repeat dose toxicity	Species	Rat
	Vehicle	Diet
	Dose	25, 50, 100, 200, 400, 800ppm [3)]
	NOAEL	-
	Effects	Almost all rats in 200ppm and higher dosage groups showed slight biiary duct cell hypertrophy.
90 days repeat dose toxicity	Species	Dog
	Vehicle	Diet
	Dose	1.5, 3, 6 mg/kg [3)]
	NOAEL	-
	Effects	Loose stolls were noted among 6, 3 and 1.5mg/kg after three, six and nine weeks respectively.
2 years repeat dose toxicity	Species	Dog
	Vehicle	Diet
	Dose	0.75, 3, 6mg/ka/day [4)]
	NOAEL	0.75mg/kg/day
	Effects	Residual tin remained in the tissue of exposed animals and brown discoloration of the serosal surface of the small intestine occurred at 3mg/ka/day. A reduction in urinary copper output was observed at 0.75mg/kg/day or more.
2 years repeat dose toxicity	Species	Rat
	Vehicle	Diet
	Dose	0.75, 3, 6, 12mg/kg/day [4)]
	NOAEL	3mg/kg/day
	Effects	An increased incidence of cysts of the liver and pituitary gland of female was observed at 12mg/kg/day. A slight decease of food intake and a related mild depression of growth rate were observed during the first three months.
Reproductive and developmental toxicity	(Rabbit teratology study at 05, 1.5, 3mg/kg/day) [5), 7)] An increase in the occurrence of dilation of the third and/or lateral ventricle of the brain was noted at 3.0mg/kg/day. A high incidence of folded retains was noted at 0.75mg/kg/day though the significance of the Incidence was uncertain. There was no evidence of hydrocephaly at 0.75mg/g/day. (Rat reproduction study at 0.1, 0.5, 6.0mg/kg/day) [5), 7)] A decreased body weight gain was observed in females at 0.5mg/kg/day. Reproductive parameters were unaffected except for reduced post-natal pup weight gain at 6mg/kg/day. There was no evidence of induced abnormal development of pups *in utero.* NOAEL was 0.1mg/kg/day. (Rat reproduction study at 10, 30, 100ppm) [5) ,7)] A deceased body weight gain in pups during lactation, and reduced survival of F_0 and F_1 offspring were observed at 30mp. NOAEL was 10ppm (0.7mg/kg/day).	

Carcinogenicity	(Rat 2years carcinogenicity study at 1, 3, 6mg/kg/day) [6] An increase of the number of benign or malignant tumor were not observed, The incidence of focal bile hyperplasia was increased in a dose-dependent fashion and was statistically significant at all dose levels.
Kinetics and metabolism	A blood levels of tin peaked in 3-4 hrs and then declined almost to control values in 24hrs in rats. In pregnant rabbits administered 3.0mg/kg/day on days 6-18 of gestation, maternal blood tin levels peaked in 3hrs. Tin half-life in maternal blood was 8.17±1.59hrs. Tin levels in amniotic fluid, placentae and pups were increased on day 19. By day 26, tin levels in treated animals were comparable to those in control animals, except in brain where levels were slightly elevated. [5]
Effects on man	Non-irritant [2] Not a shin-sensitizer [2]

Effects on organisms in the environment	Fish	Rainbow trout	6ppb [2]
		Bluegill	4ppb [2]
	Crustacea	Daphnia	0.2g/l [2]
	algae	-	
	insect	-	

Environmental levels	Media	Fiscal year	Number of detections / number of samples	Range of detection	Limit of detection	Limit of quantitation
	water	1986	0/30 [8]		2ppb	-
	sediment	1986	0/18 [8]		0.04ppm	-
	shellfish					
	Fish					
	birds					
	Air					
	air					

REFERENCES

1) Technical information (Oxon Italia)
2) Cyhexatin (Plictran) Chemical Fact Sheet 6/85 (Cornell University, 1985)
3) WHO Pesticide Residues Series 3 (JMPR 1973)
4) AGP:1970/M/12/1 WHO/FOOD ADD/71.42 (JMPR 1970)
5) Pesticide residue in food: 1991 evaluation Part II Toxicology (JMPR 1991)
6) Pesticide residue in food: 1978 evaluations (JMPR 1978)
7) Pesticide residue in food:1994 evaluation Part II (JMPR 1994)
8) Chemical Risk Information Platform (national Institute of Technology and Evaluation)

Description of toxicological properties of Cyhexatin

) Toxicological properties

ADI: 0.007mg/kg/day (JMPR 1994)

(Rat, 24month oral repeated dose toxicity) increase of cysts of the liver and pituitary gland at 12mg/kg/day
(Dog 24month oral repeated dose toxicity) Residual tin in the tissue and brown discoloration of the serosal surface of the small intestine at 3mg/ka/day
(Rat two-generation reproduction toxicity study) A deceased body weight gain in pups during lactation, and reduced
survival of F_0 and F_1 offspring at 30ppm
(Rabbit teratology study) a high incidence of folded retains at 0.75mg/kg/day

Another support document for toxicity
LD50 Oral: 143mg/kg (male), 85mg/kg (female)
LD50 Oral: 970mg/kg (male), 1150mg/kg (female)

Risk or hazard evaluation

Teratology studies in rats and rabbits indicated that cyhexatin was teratogenic and it was found that it could not establish NOAEL from the result. Therefore, it was assessed that the ADI be withdrawn taking account of the result on Food Sanitation Investigation Council of Ministry of Health and Welfare in 1994.