CASWELL #. 345 9/16/83

THIONAZIN INSECTICIDE/NEMATOCIDE SI CLASS V

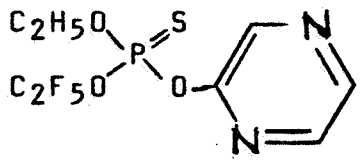
CFR References: 40 CFR 180.264, 180.3(a) and (e)5.

Chemical Name: O,O-Diethyl O-pyrazinyl phosphorothioate (CAS No. 297-97-2).[1]

Trade Names: Zinophos®, Zenophos®, Nemaphos®, Nemafos®, Cynem®.[2,3]

Common Name: thionazin (BSI).[3]

$C_8H_{13}N_2O_3PS$



Molecular Weight: 248.26[4]

Physical State: clear to pale yellow liquid (pure), amber liquid (technical).[1,4]

Melting Point: -1.7°C (pure).[4]

Boiling Point: 80°C (pure).[4]

I. Exposure and Use Factors

A. Production/Usage Volume: The registration of thionazin was cancelled voluntarily by the manufacturer, American Cyanamid, during January, 1976. Since no pesticides containing thionazin are presently registered with EPA, current domestic usage is highly improbable.[5] Some small production has continued for export only.[6]

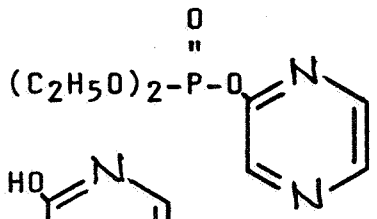
B. Chemistry

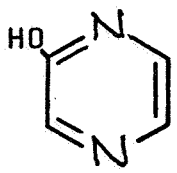
1. Solubilities: 1140 ppm in water (25°C), miscible with most organic solvents.[4,7]

2. Stability: Decomposes over a period of weeks to months. The initially clear amber liquid darkens due to decomposition, eventually becoming a black, semi-solid material.[7]

3. Manufacturing Process/Impurities: Thionazin is made by the phosphorylation of sodium pyrazinolate in an aqueous reaction medium. Technical product is about 90% thionazin.[7]

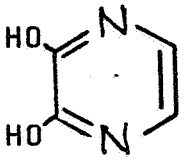
4. Degradation: Initial oxidation gives the oxygen analog, O,O-diethyl O-pyrazinyl phosphate (I) but the primary breakdown mechanism is the hydrolysis of the ether linkage to give 2-pyrazinol (II) and diethyl phosphate (III) or thiophosphate (IV). Oxidation of the pyrazine ring yields 2,3-pyrazinediol (V) and it is theorized that further oxidation may result in ring cleavage.[8]

(I) 

(II) 

(III) $(C_2H_5O)_2\text{-}\overset{\overset{\displaystyle O}{\|}}{P}\text{-}OH$

(IV) $(C_2H_5O)_2\text{-}\overset{\overset{\displaystyle S}{\|}}{P}OH$

(V) 

5. Environmental Stability

a. Foliar Degradation/Plant Metabolism: Thionazin applied to soil and absorbed by beans and tobacco is rapidly oxidized to I or hydrolyzed to II. Hydrolysis is the primary route. Further degradation of the pyrazine ring yields a number of unidentified hydrophilic degradates, some of which are incorporated into natural tissue constituents. Evidence suggests that breakdown of II is photolytic. Maximum residue levels were reached 1-2 weeks after soil treatment. Residue half-lives were <6 weeks. EPA has concluded that plants grown in thionazin-treated soil may contain residues during the early stages of growth but are relatively free of residues when mature.[8]

b. Aqueous Degradation: No data.[9]

c. Soil Degradation: No data.[9]

d. Animal Metabolism: Thionazin administered to rats orally, intravenously, or subcutaneously at dosages up to 5.9 mg/kg was rapidly hydrolyzed to 2-pyrazinol (II) and excreted in the urine. The half-life of residues was <24 hours. Additional metabolites found in the urine included the O-glucuronides of II and V.[8]

6. Bioaccumulation Potential: In rats treated with dosages of up to 5 mg/kg, the highest residue of thionazin in any tissue sampled 48 hours after treatment was 10.3 ppm. Residue distribution in various tissues varied greatly but localization was not generally observed. The transfer of residues from feed to milk and meat is not expected to be a problem.[8]

7. Soil Mobility: No information.[9] However, due to the rapid degradation of thionazin, soil mobility would not be expected to be a problem.

8. Systemic Plant Activity: Thionazin is rapidly absorbed by plant roots and is translocated throughout the plant.[8]

9. Significant Terminal Residues: Thionazin and its oxygen analog are the residues of concern[8] and both are named in the tolerances.

10. Related Pesticides/Common Metabolites: Thionazin is one of numerous phosphorothioate pesticides but appears to be the only one to contain a pyrazinyl moiety.

C. Uses and Potential Exposure

1. Registered Uses: None since 1976.[5]

2. Tolerances (40 CFR 180.264): A "negligible residue" tolerance of 0.1 ppm is established for thionazin and its oxygen analog in or on the following: broccoli, brussel sprouts, cabbage, cauliflower, corn forage or fodder (including sweet corn, field corn, popcorn), corn grain, fresh corn including sweet corn (kernels plus cob with husks removed), cottonseed, mint, snap beans, snap bean vines, strawberries, and sugar beets (roots and tops).

   The tolerance levels reflect, generally, the limits of detection of the analytical methods used at the time of registration.[10]

3. Known Foreign Uses: The manufacturer reports a minor use on fruit in south central Europe.[6]

4. Exposure via Foods: Because the only known manufacturer voluntarily cancelled the EPA registration of thionazin in January, 1976, there appears to be no reasonable likelihood of domestic usage of thionazin at this time.

   There have been no findings of thionazin in FDA monitoring programs for pesticide residues in foods from FY 78 to date.

   Thionazin is not recovered through PAM I, 211.1; is partially (<80%) recovered through 212.1, and is completely (>80%) recovered through 232.3.

5. Other Exposure Routes: Because the registration was cancelled[5] and sale and distribution have been discontinued in the U.S., dermal and inhalation exposure to thionazin would not be expected to be of concern at this time.

II. Toxicity

A. Acute Oral LD_{50}:
   Rat 12 mg/kg b.w.[11]

B. Oncogenicity: No data.[11]

C. Mutagenicity: No data.[11]

D. Teratogenicity/Reproductive Effects: No data.[11]

E. Other Acute and Chronic Effects: Rats fed technical thionazin for 31 days showed no effects at 1 ppm. At 5 ppm, plasma and red blood cell (RBC) cholinesterase inhibition were seen.[11]

   In a 90-day rat feeding study, plasma and RBC cholinesterase inhibition were noted at 8 ppm but not at 2 ppm. Also, growth depression was found at 50 ppm but not at 8 ppm.[11]

   In a 90-day dog feeding study, plasma and RBC cholinesterase inhibition were seen at 2 ppm but not at 0.5 ppm. In addition, a slight body weight loss was noted at 8 ppm but not at 2 ppm. Anemia developed at 25 ppm.[11]

F. ADI (EPA): Not established.[11]

G. ADI (FAO/WHO): Not established.

H. RPAR Status: None issued.

III. Overall Appraisal: Thionazin is highly toxic on an acute basis. The parent, thionazin, has been shown to be a strong cholinesterase inhibitor and it is expected that the oxygen analog

would also be. There are data gaps in the oncogenicity, mutagenicity, teratogenicity, reproductive effects, and chronic effects testing.

While tolerances for thionazin remain in the CFR, the manufacturer voluntarily cancelled the registration by EPA in January, 1976 and has discontinued sale and distribtion in the U.S. Hence, there is presumed to be no domestic use of thionazin and there have been no findings in FDA monitoring since FY 78.

Thionazin decomposes in a period of weeks or months in storage; thus the shelf life for unused stocks is limited.

In plants, the residue half-life was <6 weeks; in animals, it was <24 hours.

IV. Surveillance Index Classification: Class V. "Very little potential hazard, due to low toxicity or minimum possible exposure, warrants exclusion of the pesticide from routine monitoring efforts at this time."

Justification: The manufacturer cancelled the registration and discontinued distribution of thionazin in the U.S. over seven years ago. Hence, the leftover stocks, if any, would be presumed degraded beyond usefulness as a pesticide at this time. Some very minor foreign usage is reported but, because there is no significant importation of fresh fruits from the area indicated, no exposure problems are foreseen. With all known factors considered, there appears to be a minimal potential for human dietary exposure at this time.

V. Necessary Action: None.

References

1. Wiswesser, W.J. (Ed.), Pesticide Index, 5th ed., Entomological Society of America, College Park, MD (1976) p. 223.

2. Packer, K. (Ed.), Nanogen Index, Nanogens International, Freedom, CA (1975) p. 100.

3. Berg, G.L. (Ed.), Farm Chemicals Handbook, Meister Publishing Co., Willoughby, OH (1983) p. C 259.

4. Windholz, M. (Ed.), The Merck Index, 9th ed., Merck & Co., Rahway, NJ (1976) p. 1206.

5. Economic Analysis Branch, Benefits and Field Studies Div., EPA, "Preliminary Quantitative Usage Analysis of Zinophos," March, 1982.

6. Private communication, August 17, 1983.

7. Martin, J. (Ed.), Pesticide Manual, British Crop Protection Council, Worcestershire, England (1971) p. 442.

8. "Thionazin; Insecticide, Nematicide," prepared for EPA by Dynamac Corp., Rockville, MD, 8/9/83.

9. Environmental Fate Branch, Hazard Evaluation Div., EPA, "FDA/EFB Surveillance Index Profile: Zinophos," 1/19/83.

10. EPA Petition Files. (Company information has confidential status; files used only to corroborate published data or to cite EPA conclusions.)

11. Hazard Evaluation Div., EPA, "Surveillance Index Support Document, Toxicity Summary: Zinophos, Cynem," 6/17/82.

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