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MEMORANDUM

SUBJECT: Propoxur - Review of Pesticide Poisoning Incident Data

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The following data bases have been consulted for the poisoning incident data on the active ingredient propoxur (PC Code: 047802):

1) OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992.

2) Poison Control Centers - as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate and carbamate chemicals. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from 70 centers at hospitals or universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

3) California Department of Food and Agriculture (replaced by the Department of Pesticide Regulation in 1991) - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship,and number of days off work and in hospital are provided.

4) National Pesticide Telecommunications Network (NPTN) - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories humans, animals, calls, incidents and others.

PROPOXUR REVIEW

I. IDS

A total of 75 incident reports were reviewed and tabulated. Table 1 presents the number of cases per species and the illness types. In addition to these cases, there were three reporting product defects or lack of efficacy and one which contained a literature article.

Table 1: Incident Data System Reports on Propoxur by Species and Illness Type[a]

| Species | No. Incident Reports | No. Individuals Involved | Illness Type | | | |
|---|---|---|---|---|---|---|
| | | | Systemic | Dermal | Ocular | Death |
| Human | 22 | 91[b] | 84[b] | 6 | 3 | - |
| Animal[c] | 2 | 2 | 2 | | | |
| Canine | 26 | 27 | 17 | 1 | - | 16 |
| Feline | 21 | 26 | 21 | - | - | 11 |

a Multiple illnesses may be reported for each case
b One report involved 23 Casino employees who had various symptoms after the hotel in which they were working was treated for roaches. Another incident involved 47 people who sought medical attention after a California apartment building was treated. (This case is likely a repeat of the one reported in the California data review which follows.)
c Two reports contained summary data which identified species only as animal.

As noted under Table 1, two of the human incidents involved 70 people. Systemic illnesses were reported for all of them. The 23 Casino employees reported headaches, bloody noses, depression, anxiety attacks and breathing problems. The 47 apartment dwellers complained of headaches, nausea and respiratory irritation. It

should be noted that there were four IDS reports of ingestion in humans; three involved ant killer bait. The reports were summary data only and the ages of the humans were not stated.

Of the incidents involving animals, 20 in dogs and 17 in cats occurred after exposure to propoxur flea collars. Of these, death was reported in 15 dogs and 9 cats. Of those animals which died, 7 dogs and 3 cats were found with the collar bridled in their mouth. In a January 17, 1996 letter, Sandoz Agro, Inc. stated that from November 1, 1990 to November 25, 1995, the company received 25 incidents. It was estimated that 8 million collars were sold during this time period which represents 1 incident per 320,000 cases. In addition, the Sandoz veterinarians concluded that some of the incidents were unrelated to collars. The letter further states that the product label instructs users how to properly fit collars and warns against use with other pesticides and on sick or convalescing animals. However, in light of ongoing stewardship efforts, they will be submitting to the Agency proposed changes in the product labeling that will be designed to better help users avoid loose-fitting collars and thereby reduce the possibility of bridling incidents. In addition, they plan to develop an instructional video that will be provided to retail distributor's demonstrating the proper technique for fitting animals with the collar.

Additional information on propoxur exposure in domestic animals is available in the veterinary literature. In 1986, the National Animal Poison Control Center (NAPCC) reported 155 canine cases of propoxur exposure, tenth on a list of top generics; 16.8% of cases were judged toxicosis or suspected toxicosis.[1] (Categories are toxicosis, suspected toxicosis, doubtful, exposure, information and other.) There were 45 feline calls, fourteenth on the list; 37.7% were judged as toxicosis or suspected toxicosis. These statistics illustrate the greater likelihood that cats will develop clinical signs of toxicity after exposure. Cats are known to be more suspectable to carbamate compounds than dogs.[2] A majority of the canine calls involved exposure to ant traps which contain such a small amount of propoxur that risk is negligible for dogs and cats. The NAPCC published a list of the top 25 generic agents involved in calls during the 1992 calendar year.[3] (The term agent refers to any potentially toxic material including, but not limited to, veterinary and human drugs, household products, plants and

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[1] Beasley, V.R., Trammel, H.L. Incidence of poisonings in small animals. *In* Kirk, R.W. (ed.): Current Veterinary Therapy X. Philadelphia, W.B. Saunders, 1989, pp. 97-113.

[2] Reid, F.M. and Oehme, F.W. Toxicoses. *In* Sherding, R.G. (ed.): The Cat: Diseases and Clinical Management. New York, Churchill Livingstone, 1989, pp. 185-215.

[3] Buck, W.B. Top 25 Generic Agents Involving Dogs and Cats Managed by the National Animal Poison Control Center in 1992. *In* Bonagura, J.D. (ed.): Current Veterinary Therapy XII. Philadelphia: W.B. Saunders Co., 1995, p. 210.

pesticides.) For the 12,611 calls involving one or more dogs, propoxur ranked ninth on the list. For the 5351 cases involving one or more cats, propoxur was thirteenth.

II. Poison Control Center Data

Propoxur was not one of 28 chemicals for which poison control center data were requested. Although propoxur is a carbamate, it is not used agriculturally and therefore was not included in the Data-Call-In.

III. California Data - 1982 through 1993

Detailed descriptions of 293 cases submitted to the California Pesticide Illness Surveillance Program were reviewed. Ninety (90) involved exposure to propoxur alone. In 62 cases, there was exposure to propoxur in combination with petroleum distillates and/or butoxyethanol, but propoxur was judged to be responsible for the reported illness. This total of 152 cases was reviewed for the following analyses. Table 2 presents the illness categories and number of days of disability and hospitalization by year.

Table 2: Types of Illnesses and Days of Disability and Hospitalization Reported as a Result of Propoxur Exposure in California, 1982-1993

| Year | No. of Cases | Days of Disability (No. of Cases) | Days of Hospital. (No. of Cases) | Illness Type[a] | | | |
|---|---|---|---|---|---|---|---|
| | | | | Systemic | Eye | Skin | Total |
| 1982 | 11 | 1 | - | 8 | 3 | - | 11 |
| 1983 | 15 | 34 (4) | 26 (2)[b] | 10 | 4 | 1 | 15 |
| 1984 | 11 | 4 (2) | - | 6 | 4 | 1 | 11 |
| 1985 | 24[c] | 8 (7) | - | 24 | - | - | 24 |
| 1986 | 7 | 1 (1) | - | 5 | 2 | - | 7 |
| 1987 | 0 | - | - | - | - | - | 0 |
| 1988 | 11 | 17 (4) | - | 7 | 3 | 1 | 11 |
| 1989 | 7 | 8 (1) | - | 6 | 3 | - | 9 |
| 1990 | 7 | 10 (1) | - | 3 | 2 | 2 | 7 |
| 1991 | 48[d] | 5 (1) | - | 48 | 9 | 8 | 65 |
| 1992 | 6 | 35 (6) | - | 4 | 2 | - | 6 |
| 1993 | 5 | 2 (1) | - | 4 | 1 | 1 | 6 |
| Total | 152 | 125 | 26 | 125 | 33 | 14 | 172 |

a More than one illness category may be reported for each case
b Included one teenager who was hospitalized 19 days after an attempted suicide; the majority of the time in the hospital was for psychiatric care
c Includes two episodes involving 15 employees who were present during a crack and crevice treatment and 5 office workers who developed symptoms after the outside of their building was treated
d Includes 44 residents and the applicator who became ill after an apartment complex was treated for roaches

Of the 125 persons who had systemic illnesses, 63 (50.4%) had symptoms involving the respiratory system, including coughing, tightness in the chest, shortness of breath and congestion. It was noted in the Comments sections of the reports that personal protective equipment (goggles) was not worn in 4 cases, a Notice of Violation or Warning was issued in 6 cases and there was a label violation in 1 case.

The data were also tabulated by exposure category; the results appear in Table 3.

Table 3: Activity Categories for Propoxur Exposure in California, 1982-1993[a]

| Year | Exposure Category | | | | | | |
|---|---|---|---|---|---|---|---|
| | Appl | Resistru | Resinon | Drift | Other | Othernon | Expotoconc |
| 1982 | 4 | 5 | - | - | | 2 | - |
| 1983 | 5 | 5 | - | 2 | - | 3 | - |
| 1984 | 5 | 2 | - | - | - | 4 | - |
| 1985 | - | 22 | - | - | - | 1 | 1 |
| 1986 | 2 | 3 | - | - | 2 | - | - |
| 1988 | 4 | 6 | - | - | - | - | 1 |
| 1989 | 1 | 4 | - | 1 | - | 1 | - |
| 1990 | 3 | 2 | - | 1 | - | 1 | - |
| 1991 | 3 | 1 | 44 | - | - | - | - |
| 1992 | 1 | 1 | - | 2 | 2 | - | - |
| 1993 | 2 | 1 | - | 2 | - | - | - |
| Total | 30 | 52 | 44 | 8 | 4 | 12 | 2 |

a Year 1987 had no poisoning reports
Appl = applicator; Resistru = worker exposed to residue of structural treatment; Resinon = non-occupational residue exposure; Drift = exposure to pesticide that has drifted from intended targets; Other = other occupational exposure; Othernon = non-occupational miscellaneous exposure; Expotoconc = exposure to pesticide after manufacture and prior to use (e.g. warehouse, transport)

## IV. NPTN

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991, inclusively, propoxur ranked number 11. During this time period, there were 1782 calls reporting 455 incidents in 331 humans, 58 animals and 66 others.

## V. LITERATURE REPORTS OF HUMAN POISONINGS

Ames *et al* conducted a study of occupational exposure to flea control products among California pet handlers.[4] Propoxur was associated with an increased frequency of convulsions, muscle twitching, unusual tiredness, headaches and burning eyes. In response to the study, the state of California notified EPA that it is considering placing all pesticide products formulated as dips and shampoos for use on dogs and cats into its reevaluation

[4] Ames, R.G., Brown, S.K., Rosenberg, J., Jackson, R.J., Stratton, J.W. and Quenon, S.Q. Health Symptoms and Occupational Exposure to Flea Control Products among California Pet Handlers. Am. Ind. Hyg. Ass. J. 50(9):466-472 (1989).

process.[5] The reason for the concern is the number of illnesses by applicators as a result of being dermally exposed to these products.

Baron summarized reports of three suicide incidents.[6] In one case, a 36-year-old man was thought to have ingested 200 ml of a propoxur formulation of unspecified concentration. He died after 5 days without gaining consciousness. In the second case, a 32-year-old man survived ingestion of what was thought to be 150 ml of an unspecified formulation. He responded to small doses of atropine. In the third case, a comatosed 39-year-old woman was brought to the emergency room with pinpoint pupils that were unresponsive to light, white frothy secretions from the mouth and rales, wheezes and rhonchi in the chest. Although RBC and plasma cholinesterase levels were within normal limits, propoxur and its main metabolite were found in a gastric aspirate 18 hours after admission. She recovered but only identified the ingested material as an "unknown insecticide".

Baron also cites some studies on human volunteers. A 42-year-old male ingested 1.5 mg/kg body weight of propoxur. RBC cholinesterase activity was minimum (27% of normal) 15 minutes after administration. By about 20 minutes post administration, he developed blurred vision and nausea which were followed by vomiting, sweating and an increased pulse rate. One hour after administration, he was feeling better and sweating less but was still nauseated and tired. RBC cholinesterase was 95% of normal two hours after administration. In another study, a single 0.36 mg/kg dose of propoxur precipitated a fall in RBC cholinesterase to 57% of normal within 10 minutes. Clinical symptoms included abdominal discomfort, blurred vision, moderate facial redness and sweating which lasted about 5 minutes. RBC cholinesterase recovered within 3 hours. Volunteers which received dosages up to 0.20 mg/kg every half-hour for a total dose of 1.0 mg/kg had no symptoms, even though their RBC cholinesterase levels were just as affected as in the previous report. In another study, volunteers who took doses of up to 1.6 mg/kg before going to bed reported no effects.
In a dermal exposure study, a 4-hour exposure at an average concentration of 3 $mg/m^3$ had no effect on four volunteers and did not inhibit RBC or plasma cholinesterase.

In a study of the active ingredients identified with childhood ingestions of pesticides, 554 propoxur cases were reported to the

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[5] Correspondence from Elin D. Miller, Chief Deputy Director, Department of Pesticide Regulation, California EPA to Susan H. Wayland, Deputy Director, Office of Prevention, Pesticides and Toxic Substances, March 25, 1994.

[6] Baron, R.L. Carbamate Insecticides. *In* Hayes, W.L. and Laws, E.R. (eds.) Handbook of Pesticide Toxicology. Volume 3 Classes of Pesticides. New York, Academic Press, 1991.

Poison Control Centers in 1989.[7] Comparisons to other chemicals and use information are in the following section.

## VI. USE INFORMATION

The 1990 National Home and Garden Pesticide Use Survey is a cross-sectional survey of the pesticides used in and around homes. It was estimated that 21,484,000 containers (6.6% of all pesticides) of propoxur were available in U.S. households. On a list of the mostly frequently found pesticides in the home, propoxur ranked number four. The percentage of homes which had propoxur products was 23.7%.

The number of childhood ingestions of propoxur reported to the Poison Control Centers in 1989 was compared to the amount of propoxur containers in homes in 1990.[7] There were 25.8 cases of childhood ingestions per million containers which was lower than the median of 40.0 for 83 chemicals in the study.

## VII. CONCLUSIONS

1. As of April 1, 1996, there were 75 incidents reported to the Incident Data System. (See Table 1.) Of these, 22 reports involved 91 humans; a total of 70 individuals were exposed in two incidents. The vast majority of the illnesses reported were of a systemic nature. There were 26 reports involving 27 dogs and 21 reports involving 26 cats. Of these, 20 cases in dogs and 17 in cats involved flea collars. Death was the final outcome in 15 dogs and 9 cats; of these, 7 dogs and 3 cats were found with the collar bridled in their mouth. In a January 17, 1996 letter, Sandoz Agro, Inc. stated that they will be submitting to the Agency proposed changes in the product labeling that will be designed to better help users avoid loose-fitting collars and thereby reduce the possibility of bridling incidents. In addition, they plan to develop an instructional video that will be provided to retail distributor's demonstrating the proper technique for fitting animals with the collar. Data in the veterinary literature from the National Animal Poison Control Center consistently have propoxur among the top 15 generic chemicals involved in poisonings of dogs and cats.

2. Detailed descriptions of 152 cases from the California Pesticide Illness Surveillance Program, 1982-1993, were reviewed and tabulated. These cases involved exposure to propoxur alone or in combination with petroleum distillates and/or butoxyphenol in which propoxur was judged to be responsible for the illness. (See Table 2.) The majority of the illnesses were of a systemic nature. Of the 125 persons who had systemic illnesses, 63 (50.4%) had symptoms

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[7] Blondell, J.M. Relationship between pesticide toxicity and poisoning occurrence in children five and under in the United States. A dissertation submitted to George Mason University, Fairfax, Virginia, 1994.

referable to the respiratory system, including coughing, tightness in the chest, shortness of breath and congestion. The three main activity categories associated with the 152 incidents and the number (percentage) involved were as follows: 1) worker exposed to residue of structural treatment - 52 (34%); 2) non-occupational residue exposure - 44 (29%); 3) applicator - 30 (20%).

3. On the list of the top 200 chemicals for which NPTN received calls from 1984-1991, inclusively, propoxur ranked number 11. During this time period, there were 1782 calls reporting 455 incidents in 331 humans, 58 animals and 66 others.

4. According to the National Home and Garden Pesticide Use Survey, propoxur is ranked number four on a list of pesticides most frequently used in the home. In a study of the active ingredients identified with childhood ingestions of pesticides, 554 propoxur cases were reported to the Poison Control Centers in 1989. Comparing the number of ingestions to the use data, there were 25.8 cases of childhood ingestions per million containers which was lower than the median of 40.0 for 83 chemicals in the study.

## VIII. RECOMMENDATIONS

1. Proposed labeling changes recommended by Sandoz Agro, Inc. designed to fit flea collars properly are appropriate and should be adopted.

2. Products likely to be used in office buildings or other areas where many people may be present should have a label warning advising unprotected persons to vacate the area being treated and to avoid contact with them until the treated areas have dried.