UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 14 1992

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Critique of Key Human Studies on Aldicarb Watermelon Contamination Report INTRA-0301

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I. Introduction

At your request of December 5, 1991, I have reviewed the November 22, 1991 Rhone-Poulenc Ag Company submittal by Rothman, Pastides and Cole entitled "Review of Goldman et al. Analysis of Aldicarb Exposure Following Illegal Use on Watermelon and Cucumbers."

The other aldicarb poisoning epidemiology publications, background memos from you, and the mass hysteria publications that I also reviewed are discussed under Detailed Considerations. I used this material to formulate the questions in the attachment.

You requested that I do three things:

1) review and comment on the critique;

2) recommend outside experts who could provide medical epidemiology or medical statistics advice on the key studies; and,

3) provide you with questions to be addressed by outside experts in medical epidemiology, or medical statistics.

Item 1 above is given below, and organized around three key topics in the critique: epidemiologic study methods, case definitions/ case ascertainment, and threshold dose.

Item 2, a list of experts in medical epidemiology and medical statistics, and Item 3, suggested questions, are included as Attachments A and B.

Per our discussions, I have also attached several data tables on aldicarb poisonings compared to other carbamate poisonings in California agricultural workers and pesticide handlers. These data in Attachment C were prepared recently by our Branch staff for another Agency Workgroup on Organophosphate/Carbamate Strategy.

These data will give you some perspective on agricultural poisonings in California workers for the period 1982-1989. Please note that aldicarb represents the highest number of hospitalized cases of seven leading carbamates.

The data should be considered draft since the workgroup deliberations are still in progress and table formats may change. The numbers have been checked for completeness and accuracy, as reported to the Agency from the California Pesticide Illness Surveillance Program.

Conclusions/Recommendations

To address the questions raised by Rothman et al, 1991, about the differences between case definitions and case ascertainment during an epidemic and during an epidemiological study, I recommend that you consider obtaining an up-to-date chemical specific report on aldicarb poisonings from the National Association of Poison Control Centers.

Jerry Blondell and I would be happy to help you draft a specific request. The report should include a summary for all treated cases, as well as summary statistics. From recent discussions with the Poison Control Center staff for the National Association of Poison Control Centers, poisoning case data for the years 1985 to the present would be most helpful for your purposes.

I also recommend we consider a formal meta-analysis on all published aldicarb poisoning data after we have the findings from the poison control center data. Also, I recommend that we request any clarification that Lynn Goldman et al. can provide for the dosage estimates for Table 2, p. 145 of the 1990 May/June paper.

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Detailed Considerations

The paper to be reviewed here is a critique of Goldman et al 1990 by members of The Epidemiology Resources Inc. of The New England Epidemiology Institute. The critique was written at the request of Rhone-Poulenc Ag Company, and submitted to the Agency in support of the Aldicarb Pesticide Registration EPA REG. No. 264-330.

In earlier correspondence to the Company, the California State Health Department noted on October 15, 1990 that it would be useful to obtain the assistance of an epidemiologist to interpret the California analyses reported in two publications (see References) by Goldman et al., 1990, entitled:

1) "Pesticide Food Poisoning from Contaminated Watermelons in California, 1985" and

2) "Aldicarb Food Poisonings in California, 1985-1988: Toxicity Estimates for Humans."

Epidemiology Study Methods

Rothman et al., 1991, address a number of concerns about the case definition and case ascertainment methods. Since poison control center data are collected by trained medical personnel, these data should provide a basis for comparison with the epidemics, and signs and symptoms of aldicarb poisoning reported in California and elsewhere.

The incidence of aldicarb poisoning is relatively high per thousand applications, according to CA data on worker poisonings. Mary Clock, who recently joined the OREB staff, has prepared tables from the CA data for the OP Strategy Workgroup, and a draft of this information is attached for your review. The poison control center data covers over 70% of the United States, and it represents a better picture of trends on reported poisonings due to aldicarb.

Correctly, Rothman et al., 1991 point out that the report of an epidemic is different from a carefully designed and executed epidemiologic study. But, this fact does not make epidemic report data useless or irrelevant for regulatory purposes. On the contrary, the epidemic reports, and especially the epidemic curve in the first Goldman et al, July/August 1990 paper, Fig.1, p. 233, suggest that the watermelon aldicarb illness reports are real and very significant from the standpoint of protection of public health.

The index case was identified by medical authorities on July 3, 1991. Prior cases were subsequently identified by the State Health Department. There was a significant increase in the number of probable cases prior to that date. In other words, the epidemic was already in progress when the first case came to medical attention. Therefore, the mass hysteria hypothesis is not logical. The bulk of the probable cases happened before media attention.

Mass Hysteria

A review of the five mass hysteria papers suggests that the California epidemic does not fit the pattern of reported cases of mass hysteria in: an elementary school chorus, Small and Borus, 1983; a North Carolina elementary school Cole, 1990; and, an industrial setting, Hall and Johnson, 1989. In the latter report, victims were sewing machine operators working under rigid work rules and a stressful work environment. In these three situations, cases were more often friends, and no chemical agent was linked to the symptoms. Psychosocial factors may have been mixed with physical factors to produce the reported symptoms.

In Cole, 1990, there was an absence of laboratory results and physical findings confirming a specific organic cause. Children were affected, but adults in the same environment were not affected.

This pattern is in sharp contrast to the CA situation where the index case was a 62-year-old women on digoxin therapy who ate contaminated watermelon, and presented at the emergency room within 30 minutes with serious illness. She had hypotension, severe bradycardia (31 beats per minute [bpm]), atrial fibrillation, diaphoresis, vomiting, diarrhea, lacrimation, salivation, and muscle twitching, According to the first Goldman et al, 1990 report, p. 230, two other family members became ill from eating the same melon, although with milder symptoms.

Eventually 1376 illnesses were reported in California, with over 70% classified as probable cases of aldicarb poisoning from eating contaminated watermelon. In Oregon, one day after the California case, an unrelated case was reported to Oregon State Health officials. Subsequently, 264 reports were received, and 61 definite cases were identified.

In general, this points out that symptoms of pesticide poisoning may vary among people depending on how much they ate and variations in their general health status. Such variation in reported symptoms was also evident in the cucumber poisoning reports, Goes et al., 1990, and Hirsch, et al., 1987.

Finally, the two unanswered questions in Singer, 1982 are of interest, here. How does mass psychogenic illness start and why is it not more common?

Threshold dose, dose-response and related toxicology

Data on dose-response, dosage estimates, and related toxicology are scattered throughout the several epidemic reports. I have marked the information in each report, but not repeated them here. I recommended above that we consider a formal meta-analysis to highlight range, variability, and consistency among the various sets of published data.

Dose estimates could vary for several reasons. First, people ate different amounts of contaminated watermelon or cucumber, with or without other food. Second, people vary in general characteristics and health status. Third, symptom reports vary, and there may be concurrent illness of viral or bacterial origin. To address these problems the California watermelon report used the case definition of diarrhea or nausea/vomiting within 2 hours of watermelon consumption. Sensitivity for this case definition was 79% and specificity was 82%.

Papers reviewed

I have also reviewed the following related items to form my conclusions:

a) four papers referenced in the Company review on mass hysteria--
Cole et al., 1990, North Carolina/elementary school;
Gann, 1990, comments on Cole, 1990;
Hall et al., 1989, review article/industrial settings
Small and Borus, 1983, Massachusetts/elementary school
Singer, 1982, review article/general

b) two papers by Goldman et al., May/June, 1990, and July/August, 1990, California/watermelon ;

c) related aldicarb poisoning publications--
Goes et al., 1980, Nebraska/cucumbers;
Green et al., 1987, Oregon/watermelon;
Hirsch et al., 1987, Canada/cucumbers;

d) correspondence to the Company by Goldman dated October 15, 1990; and,

e) reviews of an earlier draft of the Goldman papers by Jerome Blondell and yourself.

A complete list of references follows.

cc: Ruth Allen
Jerome Blondell
Chemical File: Aldicarb
Correspondence
Circulation

Aldicarb References

Goes, E. A., et al. Suspected Foodborne Carbamate Pesticide Intoxications Associated with Ingestion of Hydroponic Cucumbers. American Journal of Epidemiology 1980 [Vol. 111, (No. 2)] pp. 254-260.

Goldman, L. R., et al. Pesticide Food Poisoning from Contaminated Watermelons in California, 1985. Archives of Environmental Health July/ August 1990 [Vol. 45 (No. 4)] pp. 229-236.

Goldman, L. R., Beller, M., and Jackson, R. J. Aldicarb Food Poisoning in California, 1985-1988: Toxicity Estimates for Humans. Archives in Environmental Health May/June 1990 [Vol. 45 (No. 3)] pp. 141-147.

Goldman, L. R. Letter to G. S. Simon, Director of Toxicology, Rhone-Poulenc Ag Company. October 15, 1990. pp. 1-5.

Green, M. A., et al. An Outbreak of Watermelon-Borne Pesticide Toxicity. American Journal of Public Health 1987 [Vol. 77 (No. 11)] pp. 1431-1434.

Hirsch, G. H., et al. Report of Illness Caused by Aldicarb-Contaminated Cucumbers. Food Additives and Contaminants 1987 [Vol. 5 (No. 2)] pp. 155-160.

Rothman, K. J., Pastides, H., Cole, P. Epidemiological Review of Goldman et al. Submitted to EPA by Rhone-Poulenc Ag Company. October 30, 1991. pp. 1-13.

Mass Hysteria (Papers Cited in Rothman et al. and also reviewed here)

Cole, T. B., et al. Patterns of Transmission of Epidemic Hysteria in a School. Epidemiology 1990 [Vol. 1 (No. 3)] pp. 212-218.

Gann, P. H. Truth or Consequences: When the Study Reintroduces the Disease Agent. Epidemiology 1990 [Vol. 1 (No. 3)] pp. 192-194.

Hall. E. M., and Johnson, J.V. A Case Study of Stress and Mass Psychogenic Illness in Industrial Workers. Journal of Occupational Medicine 1989 [Vol. 31 (No. 3)] pp. 243-250.

Singer, J. E. Yes Virginia, There Really is a Mass Psychogenic Illness. In Colligan M., Pennebaker J., Murphy L. (eds): Mass Psychogenic Illness: A Social Psychological Analysis 1982 Lawrence Earlbaum Associates, Hillsdale, N. J. pp. 127-135.

Small, G.W. and Borus, F. Outbreak of Illness in a School Chorus New England Journal of Medicine [Vol. 308 (No. 11)] pp. 632-635.