

Planning Report
for
Toxicological Research

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INTRODUCTION

Paragraph 2.4 in UBTL's contract with NIOSH reads as follows:

- 2.4. The contractor will plan acute and chronic toxicological studies on specified chemicals used in agriculture and agricultural industries. Chemicals to include but not limited to economic poisons, fertilizers, medicants for which the need for toxicological data is manifest. It is expected that this project will be a part of and utilize, in so far as practicable, the staff and facilities developed for the project for assessing the validity of pesticide field reentry safety intervals.

The problem identification approach used in the accomplishment of the objectives for this paragraph can be outlined in the following steps.

Step 1. Analysis of the ARAL agricultural accident and disease data base for priority setting of problems of agricultural workers. In reality, this meant an analysis of the California data since it constitutes the majority of the data base. This analysis was carried out and reported by Dr. Burkart in the ARAL Information Section.

Step 2. Since the data base information represented such a small portion of the nation, Mr. deGroot generated an excellent questionnaire which he hoped would add substantially to any conclusions which we might draw from the California data. Under Mr. deGroot's direction, questionnaires were sent to a number of authorities for their opinions. The analysis of these questionnaires was accomplished by Dr. Burkart in the ARAL Information Section.

Step 3. From the information generated in Step 1 and 2, several compounds were selected for detailed study. Literature searches were started on each of those compounds selected. As would be expected, a comprehensive literature review is a continuing process. To generate these bibliographic automated searches (BURT, TOXLINE, MEDLINE) and manual literature searches were made. UBTL's Dr. Ed Graham was in charge with the responsibility to combine the various searches into one comprehensive bibliography for each subject. Dr. Graham then proceeded to collect abstracts and papers

in total for review.

Step 4. Using the abstracts and articles collected by Dr. Graham, the Toxicology Staff reviews this information to identify research needs or problem areas. The criteria we set up for a research need or problem area is the following:

It is an occupational problem.

It is a problem of agricultural workers.

It is a toxicology problem.

In addition to the information generated by the Information Section for review, a number of special subjects were selected for special review. From this review would emerge a series of acute and chronic toxicological study recommendations which were pertinent and timely to the mission of the NIOSH Agricultural Occupational Health Program.

The various sections of this report follow the steps presented in this introduction.

- ARAL Information Section Priority List
- Bibliographies
- Review of Bibliographies
- Summary

**ARAL INFORMATION SECTION
PRIORITY LIST**

Expert Opinion Questionnaires

To enhance the process of identifying the most serious problems or hazards in agricultural health, the opinion of a selecte group of experts was sought. A questionnaire listing candidate diseases and hazards was prepared, along with an explanatory letter, and sent to those listed in Table I. Responses were received from seven addresses, usually without identification. The completed questionnaires were analyzed and the resulting data used in conjunction with disease frequency data to create a rank ordered list of hazardous chemicals. Dr. Burkart's priority evaluation is incorporated in this report in total and follows Table I and the questionnaire sent to the experts.

Table I

Individuals Solicited for Expert Opinion Questionnaire

Kingsley K. Kay, Ph.D.
16 Skyridge Road
Greenwich, CT 06830

Dean A. Emanuel, M.D.
Marshfield Clinic Foundation for
Medical Research and Evaluation
510 North St. Josephs Avenue
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AGRICULTURAL OCCUPATIONAL HEALTH RESEARCH
PRIORITY QUESTIONNAIRE

Introduction:

You are one of 15 experts being asked to complete this questionnaire. Since a large survey is not being conducted, your response is particularly important. A reply within three weeks will be very helpful.

Directions:

This questionnaire has two parts. Part I is a list of diseases and conditions often attributed to work in the agricultural environment.¹ Part II is a list of harmful agents often found in that environment. Based on your experience, please rank the 10 diseases or conditions and the 10 agents which merit the highest research priority. Rank Parts I and II separately, applying the 1 (highest priority) to 10 rating to each part.

In the interest of making the questionnaire a manageable size, three digit ICD codes and corresponding names have generally been used. In the ICD manual many of the coded headings are followed by further detailed listing and explanations of what is or is not included. Please use the manual while completing the questionnaire to insure an accurate response.

¹ICD codes and names are from the Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, Eighth Revision, Volume 1, 1967, World Health Organization, Geneva.

In making your judgement about priority, please keep in mind the specific goal of minimizing existing health problems in agriculture. The following criteria may help in your task:

A high priority disease or condition, or harmful agent is one which

- is usually related to occupation
- is generally confined to agriculture
- places a relatively large population in risk
- is accompanied by more than minimal effects
- is associated with a relatively high attack rate
- does not have well established methods for diagnosis, treatment, or prevention.

As a corollary to the priority ranking, there may be instances where it is your opinion that reduction of the occupational impact of a disease or hazardous agent depends not on additional research, but rather on action in the fields of education or regulation. It would be helpful if you would identify those instances in the Part I and Part II listings. Suggestions about needed changes to the lists, as well as other comments you have are welcome. A sheet has been provided for that purpose.

If you are in doubt in any way about the questionnaire, please do not hesitate to call (801 524-5590, Mr. Norman F. deGroot).

AGRICULTURAL OCCUPATIONAL HEALTH RESEARCH
PRIORITY QUESTIONNAIRE

Part I

DISEASES OR CONDITIONS

<u>ICD Code</u>		<u>Research Priority Rank*</u>
INFECTIVE AND PARASITIC DISEASES:		
003	Other Salmonella infections (See ICD Manual)	—
011	Pulmonary tuberculosis	—
021	Tularemia	—
022	Anthrax	—
023	Brucellosis	—
024	Glanders	—
035	Erysipelas	—
037	Tetanus	—
038	Septicemia	—
062	Mosquito-borne viral encephalitis	—
070	Infectious hepatitis	—
071	Rabies	—
100	Leptospirosis	—
110	Dermatophytosis	—
113	Actinomycosis	—
114	Coccidiomycosis	—
115	Histoplasmosis	—
116	Blastomycosis	—
117.1	Sporotrichosis	—
132	Pediculosis	—
133	Ascariasis	—

*From all diseases and conditions listed in Part I, only rank top 10 based on your opinion. Rank highest need as 1.

Part I

DISEASES OR CONDITIONS

<u>ICD Code</u>		<u>Research Priority Rank</u>
NEOPLASMS:		
173	Other malignant neoplasms of skin	___
216	Benign neoplasm of skin	___
DISEASES OF THE BLOOD AND BLOOD FORMING ORGANS:		
284	Aplastic anemia	___
287.1	Thrombocytopenia	___
DISEASES OF THE NERVOUS SYSTEM AND SENSE ORGANS:		
360	Conjunctivitis and ophthalmia	___
363	Keratitis	___
372	Pterygium	___
389	Other deafness	___
DISEASES OF THE CIRCULATORY SYSTEM:		
401	Essential benign hypertension	___
402	Hypertensive heart disease	___
410	Acute myocardial infarction	___
412	Chronic ischemic heart disease	___
443.0	Raynaud's syndrome	___
455	Hemorrhoids	___
DISEASES OF THE RESPIRATORY SYSTEM:		
466	Acute bronchitis and bronchiolitis	___
480-486	Pneumonia	___
491	Chronic bronchitis	___
492	Emphysema	___
493	Asthma	___
503	Chronic sinusitis	___
507	Hay fever	___

Part I

DISEASES OR CONDITIONS

ICD
Code

Research
Priority Rank

DISEASES OF THE RESPIRATORY SYSTEM (continued):

516	Other pneumoconiosis and related diseases	
516.1	Farmer's lung	---
	Bagassosis	---
	Byssinosis	---
516.2	Silo-filler's disease	---

DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE:

681	Cellulitis of finger and toe	---
684	Impetigo	---
692	Other eczema and dermatitis	
692.0	Due to detergents	---
692.4	Due to chemicals	---
692.6	Due to plants	---
692.8	Due to other specific agents	
	Hot weather	---
	Sunburn	---
703	Diseases of nail	---

DISEASES OF MUSCULOSKELETAL SYSTEM:

713.0	Osteo-arthritis	---
714.0	Other specified forms of arthritis	---

NATURE OF INJURY:

N992	Effects of heat	---
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AGRICULTURAL OCCUPATIONAL HEALTH RESEARCH
PRIORITY QUESTIONNAIRE

Part II

AGENTS

<u>Agent</u>	<u>Research Priority Rank*</u>
Heat	_____
Noise	_____
Ultraviolet light	_____
Vibration	_____
Acetylene	_____
Aldrin	_____
Ammonia	_____
Arsenic & Compounds	_____
Asphalt fumes	_____
Azinphos methyl (Guthion)	_____
Calcium arsenate	_____
Carbaryl (Sevin)	_____
Carbon dioxide	_____
Carbon monoxide	_____
Chlordane	_____
Chloropicrin	_____
Cotton dust	_____
2,4-D	_____
DDVP (Dichlorvos)	_____
Demeton (Systox)	_____
Diazinon	_____
Dibrom	_____
Dieldrin	_____
Diquat	_____

*From all agents listed in Part II, only rank top 10 based on your opinion. Rank highest need as 1.

Part II

AGENTS

<u>Agent</u>	<u>Research Priority Rank</u>
Endosulfan (Thiodan)	---
Endrin	---
EPN	---
Ethylene glycol	---
Fluoride	---
Gasoline	---
Heptachlor	---
Hydrogen sulfide	---
Lead, inorganic, fume	---
Lead arsenate	---
Lindane	---
Malathion	---
Mercury (alkyl)	---
Mercury (other forms)	---
Methyl bromide	---
Methyl parathion	---
Nicotine	---
Nitrogen dioxide	---
Paraquat	---
Parathion	---
Pentachlorophenol	---
Phosdrin	---
Pyrethrum	---
Rotenone	---
Silicon dioxide	---
Sodium fluoroacetate (1080)	---
Sulfur	---
2,4,5 T	---
Thimet	---
Temik	---
TEPP	---

Part II

AGENTS

<u>Agent</u>	<u>Research Priority Rank</u>
Tetra ethyl lead	—
Thallium	—
Toxaphene	—
2,4,6-Trinitrophenol (picric acid)	—
Warfarin	—

COMMENTS AND SUGGESTED LIST CHANGES:

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

TO : Dr. Stan Allen

DATE: 14 April 1975

REFER TO: 75IS097

FROM : J. A. Burkart

JAB

SUBJECT: Priority Listing of Harmful Agricultural Chemicals Based on Available Data Collected by the ARAL Program

Available information for priority setting is sparse and comes from two sources: the expert opinion priority questionnaire and California workmen's compensation agricultural data reported from 1970 to September 1974. The two data sources do not report chemicals in the same manner so some data manipulation was done to make them more comparable. Three priority variables were taken from each data source and combined to give priorities for each data source. Then these two sets of priorities were combined to give an overall priority rating. When two or more scores for a priority variable were the same, the rankings of those scores were averaged.

Expert Opinion Questionnaire

Seven responses were received. One of these responses did not give priorities for individual compounds but for groups of compounds so it was difficult to compare this response with others.

Table 1 shows three priority variable rankings and the overall priority ranking. The first ranking is based on the number of times a compound was mentioned in the seven questionnaires, regardless of the ranking within the questionnaire. Only those compounds that were mentioned twice or more are considered. The second ranking is based on the following scoring system for the six comparably reported responses.

Priority Rank											Compound		
											Mentioned	Not	
Priority Score	1	2	3	4	5	6	7	8	9	10	But Not	Ranked	Mentioned
	11	10	9	8	7	6	5	4	3	2		1	0

The score for a compound is the sum of the scores of that compound's ranks on all of the questionnaires. The third ranking is the same as the second except that the questionnaire using the grouped categories was also used. All items that were grouped in a particular category received the same ranking. This results in somewhat of a bias in overstating the importance of some compounds, since a greater number of compounds are mentioned.

The three sets of rankings were combined by taking the weighted average of the three rankings, giving a weight of two to the number of times mentioned and a weight of one to each of the scores. This was done because the latter two scores are essentially the same type of measure.

California Case Data

Data from 13,758 workmen's compensation cases related to agriculture which were reported from 1970 to September 1974 compose the data base. Diseases or conditions related to agricultural chemicals were tabulated. The coding of chemicals used by California tends to combine individual chemicals into categories, making the impact of some of the chemicals mentioned by the questionnaire difficult to ascertain.

Table 2 gives three priority rankings and the overall priority ranking. The first ranking is the number of conditions caused by each chemical during the reporting period, for all chemicals causing more than 10 conditions. The next two rankings are based on the severity of the conditions: percent of cases that were hospitalized and percent of cases with lost time.

The three sets of rankings were combined by taking the weighted average of the rankings, giving a weight of two to the number of cases and a weight of one to each of the severity rankings. Again this weighting was done since the two severity rankings are essentially the same type of measure. This also gives an equal balance between frequency and severity of the conditions caused by the various chemicals.

Combined Priority Listing

The rankings from the two data sources were combined to give a final priority score as presented in Table 3. A score was given for each rank based on the following scale and the scores were summed for the two data sources. For some of the items on the questionnaire it was impossible to determine the appropriate rank for the same items from the data base since they had been grouped into categories. In these cases it was assumed that the California ranking would be the same as the questionnaire ranking.

Scoring System

Rank	1	2	3	4	5	6	7	8	9	10	>10
Score	11	10	9	8	7	6	5	4	3	2	1

The final priority score gives a rough estimate of the relative importance of the compounds mentioned; however, it is not an exhaustive list and is biased towards California experience and a

selected group of experts' opinions. It is representative of where we stand with regard to information collected by the ARAL program. Case data from other states give no information on types of agricultural chemicals. In evaluating the priority score, one should not consider small differences to be significant. Attention should be paid to the 10 or 12 compounds with the highest priority score, relegating the rest of the compounds to relative equality.

Other Priority Sources

There exist two other priority listings for agricultural chemicals; however, they are not comparable to the ARAL data sources. Results are presented for inspection purpose only.

NIOSH publishes a priority list for criteria development for toxic substances but it is not based on agricultural exposure. Results are shown in Table 4 for selected chemicals.

The Community Studies Program sponsored by the EPA studied pesticide poisonings in 15 states from 1965 to 1972. These studies had no common protocol and varied from state to state and year to year by the type, method, and quantity of data collection. No agricultural chemicals other than pesticides were reported. A summary of rankings of pesticides by number of poisonings reported is given in Table 5. The data has been summarized for only those cases for which there was occupational exposure.

JAB/nc0

xc: N. F. deGroot
J. L. Gehrich
E. R. Turner

TABLE 1

Priority Listing for Agricultural Chemical
Hazards Based on the Expert Opinion Questionnaire

<u>Chemical</u>	<u>Number of Times Mentioned (N=7)</u>	<u>Rank</u>	<u>Priority Score (N=6)</u>	<u>Rank</u>	<u>Priority Score (N=7)</u>	<u>Rank</u>	<u>Combined Rank</u>
Ammonia	5	1.5	43	1	43	1	1
Parathion	5	1.5	29	2	40	2	2
Methyl Bromide	4	4	19	4	24	5.5	3
Paraquat	4	4	15	6	19	7	4.5
Pentachlorophenol	4	4	12	8	14	11	7
Thimet	3	7.5	20	3	31	3	4.5
Methyl Parathion	3	7.5	17	5	28	4	6
Phosdrin	3	7.5	13	7	24	5.5	8
Temik	3	7.5	9	10	17	8.5	9
2, 4, 5-T	2	13	10	9	17	8.5	10
Diazinon	2	13	5	12	16	10	11
Sulfur	2	13	2	13	11	13	13
Aldrin, Dieldrin, Endrin	2	13	8	11	8	15.5	13
Lindane, Chlordane	2	13	1	15	11	12	14
Lannate	2	13	1	15	9	14	15
2, 4-D	2	13	1	15	8	15.5	16

N = Number of questionnaires on which the priority variable is measured.

TABLE 2

Priority Listing for Agricultural Chemical
Hazards Based on California Case Data

<u>Chemical</u>	<u>Number of Cases</u>	<u>Rank</u>	<u>% of Cases Hospitalized</u>	<u>Rank</u>	<u>% of Cases Lost Time</u>	<u>Rank</u>	<u>Combined Rank</u>
Parathion	285	1	32	3	76	2.5	1
Sulfur	245	2	1	13	45	14	6
Carbamates	117	3	37	2	76	2.5	3
Phosdrin	83	4	39	1	84	1	2
Ammonia	51	5	14	9.5	47	12.5	7
Methyl Bromide	40	6	15	7	73	5.5	4
Phenolic Compounds	37	7	8	11	51	11	9
Chlordane, Lindane, DDT, etc.	30	8	7	12	56	9	10.5
Thimet	28	9	14	9.5	67	7	8
Systox	27	10	19	5	75	4	5
Guthion	26	11	15	7	63	8	10.5
Lead/Arsenic	22	12	23	4	52	10	12
Malathion	20	13	15	7	47	12.5	13
Endrin, Aldrin, Dieldrin, etc.	11	14	0	14	73	5.5	14

TABLE 3

Final Priority Listing for Agricultural Chemical
 Hazards Based on Expert Opinion Questionnaire and
 California Case Data

<u>Chemical</u>	<u>Questionnaire Rank</u>	<u>California Rank</u>	<u>Final Priority Score</u>
Parathion	2	1	21
Methyl Bromide	3	4	17
Ammonia	1	7	16
Paraquat	4.5	X	15
Phosdrin	8	2	14
Methyl Parathion	6	X	12
Thimet	4.5	8	11.5
Carbamates (Carbaryl, Lannate, Furadan)	>10	3	10
Phenolics (Pentachlorophenol)	7	9	8
Systox	>10	5	8
Sulfur	>10	6	7
Temik	9	X	6
2,4,5-T	10	X	4
Chlordane, Lindane, DDT, etc.	>10	10	3
Guthion	>10	10	3
Diazinon	>10	X	2
Endrin, Aldrin, Dieldrin, etc.	>10	>10	2
Lead/Arsenic	>10	>10	2
Malathion	>10	>10	2
2,4-D	>10	X	2

X = Impossible to determine rank from the way data was reported.
 Rank assumed to be the same as for the questionnaire.

TABLE 4

NIOSH Priority List for Criteria
Development for Toxic Substances

<u>Selected Substances</u>	<u>Rating (in 100,000's)</u>
Arsenic	60,000
Parathion	10,750
Methyl Parathion	4,500
Ammonia	2,700
Carbaryl	950
Malathion	750
Chlordane	300
Guthion	247.5
Dieldrin	200
Aldrin	175
Endrin	160
Systox	140
Phosdrin	125
Pentachlorophenol	116.25
DDT	95
2,4,5-T	86.25
Heptachlor	60
Lindane	50
Lead Arsenate	45
Rotenone	42.5
Thiodan	40
Toxaphene	25
Paraquat	21
Free Sulfur	20
2,4-D	12.5
Methyl Bromide	5
Pyrethrum	3.75

TABLE 5**Occupationally Exposed Pesticide
Poisonings from the Community
Studies Projects 1965-1972**

<u>Pesticide</u>	<u>Number of Poisonings</u>
Parathion	367
Methyl Parathion	268
Phosdrin	62
Delnav	54
Malathion	48
Guthion	45
Lannate	38
Thimet	22
Ethion	17
Toxaphene	14
Carbaryl	14
DDT	12
Thiodan	10
Aldrin	9
TEPP	8
DDVP	8

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REVIEW OF BIBLIOGRAPHIES

This section reflects the review effort of Dr. S. D. Allen and the recommendations presented are his and do not necessarily reflect the opinion of NIOSH, UBTL or any other organization. The recommendations are at times outside the present capability of the ARAL Toxicology Section, including such areas as: Immunology, Dermatology, Behavioral Response and Agricultural Engineering. Toxicology, however, has long been considered to be an interdisciplinary science which these reviews reflect.

BIBLIOGRAPHY REVIEW

Subject

Ethyl Parathion, Methyl Parathion, Guthion, Carboplenothion, Ethion

Facts

These insecticides by virtue of their toxicity, persistent nature, and use have been most often incriminated in cases of residue intoxication.

Recommendations

A medical surveillance program of farm workers which come in contact with crops treated with these agents should be undertaken to ascertain if current use patterns and reentry standards are protecting workers from untoward effects.

BIBLIOGRAPHY REVIEW

Subject

Anhydrous Ammonia

Facts

- 1) Workers must generally transfer the ammonia fertilizer from container to container at least three times between factory and farm.
- 2) In typical transfer operation there are usually four or more valves to open and close.
- 3) The typical farm injury affects one man hit by the vapor stream of anhydrous ammonia who usually scrambles out of the vapor path and closes a valve to shut off the flow of ammonia.
- 4) The anhydrous ammonia vapor hits the cornea of the eye, burns result, both from the ammonia itself and its temperature.
- 5) Recovery is good if the eyes are liberally rinsed with water for 15 to 30 minutes.

Recommendations

A project to redesign hoses used to transfer anhydrous ammonia is needed. Also requirements relative to emergency eye wash water supply are needed. An education program is needed.

BIBLIOGRAPHY REVIEW

Subject

Paraquat

Facts

- 1) Paraquat and related bipyridyls such as diquat and morfamquat have the unique properties of quickly killing by contact with leaf surfaces and immediate inactivation by adsorption on to clay minerals in the soil.
- 2) These compounds produce an irreversible lung fibrosis when consumed.
- 3) The pathogenesis of this syndrome is unique in toxicology medicine and has been extensively studied.
- 4) The molecular mode of action for these compounds is not known.
- 5) Numerous cases of fatal intoxication are reported, all of which have been non-occupational.
- 6) The only occupational problem relates to finger nail damage resulting from handling this product. (See Baran, Samman and Hearn).

Recommendations

- A careful look at the economics of paraquat use is needed. Can a less toxic product be used.
- Simple hygienic precautions can prevent the occurrence of the nail problems.

BIBLIOGRAPHY REVIEW

Subject

Methyl Bromide (MB)

Facts

- 1) Methyl bromide is a fumigant used in spaces, on produce, in soil and on nursery stock.
- 2) About 16 million pounds are used in the U.S. on a yearly basis.
- 3) Exposed persons experience euphoria, cheerfulness and unconcerned attitudes. Lack of judgment may follow which leads to carelessness and greater exposure. Some show chronic signs of severe mental pathology.
- 4) Examples of occupational exposure are the following:
 - An operator of an almond nut fumigation chamber.
 - A worker on an almond-sorting belt.
 - A worker who cleaned rooms after they had been fumigated.
 - A worker who was fumigating a truck load of pears.
 - A worker who opened a box-car filled with rice which had been fumigated.

Recommendations

Whereas other toxic compounds such as paraquat are very hazardous, occupational poisoning is rare. With methyl bromide occupational exposure is real. A mechanical canary to detect levels of MB as workers enter fumigated areas is needed. A OSHA regulation for this compound is needed.

BIBLIOGRAPHY REVIEW

Subject

Carbaryl: (Sevin^R, 1-Naphthyl Methylcarbamate)

Facts

- 1) Carbaryl is teratogenic: In Guinea Pigs at 300 mg/kg with one dose and the Beagle Dog at 3.125 mg/kg to 50 mg/kg bw. with daily dosing.
- 2) Carbaryl produced EEG alterations in Rhesus monkeys after, 18 months of low level exposure.
- 3) Carbaryl injected subcutaneously produces variations in "avoidance response" and "Motivation for Liquid Response" in exposed rats.
- 4) Carbaryl treated rats showed decreased performance behavior.
- 5) Carbaryl produces dystocia and contraception effects in the dogs.

Recommendations

A broad based study of Carbaryl toxicology is indicated, including: Teratogenicity Testing, Reproductive Upset Testing and Neurobehavioral Effects Testing.

BIBLIOGRAPHY REVIEW

Subject

Ethylene Dibromide (EDB)

Facts

- 1) Recommended exposure levels for EDB is 20 ppm (time weighted average concentration).
- 2) M. B. Powers, et al, on Carcinogenicity of EDB.
"We now report our findings at the termination of these studies following 62 weeks of treatment with EDB. Tumor induction was noted as early as 12 weeks with EDB. The chemical induced a high incidence of squamous cell carcinoma of the stomach on rats and mice, (in excess of 90% and 70% respectively)."
- 3) Ethylene Dibromide LD₅₀ (g/kg)
Mice .420 Female
Rats .146 Male; .117 Female
Guinea Pigs .110
Chicks .079
Rabbits .055 Female

Recommendations

Preparations such as Dowfume -EB-5 which contain EDB should be classed as carcinogens and regulated accordingly.

BIBLIOGRAPHY REVIEW

Subject

Ethylene Dichloride (1,2, Dichloroethane)

Facts

- 1) Exposure limits of 100 ppm for 7 hours/day seem adequate to protect workers from the untoward effects of Ethylene Dichloride.
- 2) Ethylene dichloride is found in Dowfume -- 75^R and Dowfume E B-5^R or EB-15^R which are widely used agricultural chemicals used as soil and grain fumigants.
- 3) Ethylene dichloride is suspected as a causative agent in various respiratory problems of grain handlers.

Recommendations

Since Ethylene Dibromide has been shown to be a carcinogen, careful observations and a epidemiology study should be conducted if any evidence comes forth which indicates this compound to be carcinogenic.

BIBLIOGRAPHY REVIEW

Subject

Pesticides and Reproductive Function

Facts

- 1) Teratogenic effects have been produced by: Demeton, Fenthion and other O.P. in mice and rats. Carbaryl in Guinea Pigs, Dogs and Rats.
- 2) Embryotoxicity has been produced by: Demeton, Fenthion and other O.P. in mice and rats. DDT, Lindane, Carbaryl, Zineb, Dipterex, Methyl Parathion, Propozin, Prometryne and Phenozon in chick embryos and rats.
- 3) Dystocia (difficult birth) has been produced by: Carbaryl in dogs.
- 4) Contractive activity has been produced by: Carbaryl in dogs.
- 5) Impotence has been produced by: A combination of agricultural chemicals in farm workers.
- 6) Mutagenicity has been observed in: Pesticide applicators during the spray seasons compared with the non-spray seasons.
- 7) Reproductive Upset (hypermenorrhea and obyomenorrhea) has been shown to occur at a higher rate in: Women farm workers in Russia when compared with controls.

Recommendations

The need for screening agricultural chemicals for reproductive upset is evident. Screening tests could include:

For Mutagenicity - The Ames Test

For Teratogenicity and Embryotoxicity - The Wilson Procedure.

For other reproductive upsets - Multigeneration Rodent Studies.

BIBLIOGRAPHY REVIEW

Subject

Pesticides and the Immune System

Facts

- 1) Sensitization to pesticides probably is much more common than is generally realized.
- 2) Ercegovich, et al.
"There is very little knowledge of patch testing with pesticides. Physicians generally are unwilling to conduct such tests because of fear and lack of understanding about the dermal toxicity of pesticides and there are no recommended methods for use by the general physician."
- 3) Cases of allergic dermatitis have been reported to be associated with these pesticides: 1) Captan, 2) Phaltan, 3) MCPA, 4) Naled, 5) CDAA, 6) Malathion, 7) DiFalatan, 8) 2, 4, 5-TB, 9) DDT, 10) Omite
- 4) Immune System interaction associated with lindane has also been reported.

Recommendations

Develop skin sensitization diagnostic kits for use by physicians to aid in the differential diagnosis of pesticide related immune responses syndromes.

BIBLIOGRAPHY REVIEW

Subject

Pesticides and The Eye

Facts

- 1) A long list of pesticides have been shown to provoke possible ocular damage by Grośz. Most cause their effect by chemical burn action.
- 2) Children chronically exposed to Parathion Malathion, EPN and Sumithion had a reduction in vision. A cause and effect relationship is suggested. (Japan) lesions included:
 - a) Narrowing of peripheral vision.
 - b) Refraction anomaly with high incidence of astigmatism.
 - c) Neuro abnormalities and EEG problems.
 - d) Disturbance in smooth pursuit motion, and pupillary sphincter movement.
 - e) Optic neuritis and or retino/choroidal atrophy.

Recommendations

- 1) The California Code which requires that those mixers and handlers who pour concentrated pesticides to wear eye protection; should be considered by other states and OSHA for national implementation.
- 2) An Education Program on eye injury, including label warnings should receive more emphasis.
- 3) General population exposure should be carefully restricted.

BIBLIOGRAPHY REVIEW

Subject

Agricultural Aviation

Facts

- 1) There is some evidence that exposure to toxic chemicals may play a contribution or casual role in crashes of aerial applicators.
- 2) Better aircraft design such as the Ag-1 developed at Texas A & M has produced a reduction in serious and fatal injuries sustained by accident-involved occupants.

Recommendations

The need for an Epidemiology Study is apparent. Aerial applicators should be prohibited from handling pesticides. This activity should be done by a second person who doesn't fly. A test such as "eye hand coordination" or "reflex response" should be made available to aerial applicators to test themselves before flying.

BIBLIOGRAPHY REVIEW

Subject

Pesticides and Neurobehavioral Function

(See also chronic effects of pesticides and pesticides and the eye).

Facts

- 1) Various pesticides have been reported to produce neuro-behavioral changes. Examples:
 - a) Diazinon induced acute confusional psychosis in a farmhand who was spraying sheep for blow-flies.
 - b) EMG examination of farmworkers who use pesticides showed a high incidence of abnormal patterns indicating disturbance in peripheral nerve and muscle function.
 - c) Dieldrin produced abnormal behavior in sheep in a Detour Behavior Test.
 - d) Central nervous system and peripheral neuropathies are reported as chronic effects of O.P. Exposure.
(See Namba)

Recommendations

Definitive cause and effect relationship studies between pesticides and neurobehavioral changes need to be studied at every level.

- a) Chronic tests in exposed rodents.
- b) Chronic tests in exposed primates.
- c) Epidemiology study in exposed worker population.

BIBLIOGRAPHY REVIEW

Subject

Chronic Effects of Pesticides

Facts

- 1) The greater incidence of leukopenia and of neurologic manifestations found among pesticide exposed individuals suggest that insecticides (O.P. and C.H.) may have some chronic effects in man. Apple growers in Canada were the test subjects.
- 2) Occasionally, persistent effects are seen following O.P. intoxication; these include:
 - Central Nervous System Effects: (EEG changes, nervousness, impairment of memory, confusion, decreased mental concentration, etc.).
 - Peripheral neuropathies; primarily shown in the chicken model but also seen in humans.
 - Effects on liver function.
 - Alterations in blood coagulation.
 - Effect on the fetus.
 - Dermatologic effects.

Recommendations

A well planned large scale, multi-year epidemiology study is strongly recommended. Another short term study would add little to what we already know.

Long term animal tests may be helpful in defining some of the chronic effects in more detail.

BIBLIOGRAPHY REVIEW

Subject

Pesticides and Cancer

Facts

- 1) N.C.I. is now (Feb. 1975) starting in-depth cancer evaluations of certain chlorinated organic insecticides. (Approximately 100-Fungicides, Herbicides, Plant Regulators and Insecticide).
- 2) Certain agricultural chemicals have been shown to be mutagenic and/or carcinogenic. (See Kay)
- 3) In one epidemiology study it was shown that there is a higher incidence of certain types of cancer in Washington State Farmers and Orchardists.

Recommendations

There is no question that agricultural chemicals need to be screened for carcinogenic properties. Since mutagenic activity correlates rather well with carcinogenic activity screening of agricultural chemicals using the Ames Test or a modification of it should be considered. N.C.I. and NIOSH should jointly decide who is going to do this work.

SUMMARY

A system was developed to define agricultural, occupational toxicology research needs and problem areas using the best available knowledge and data. Using a priority list developed by the ARAL Information Section and inputs from other sources, 10 compounds and 7 special areas of study were selected for in-depth investigation. To date bibliographies on the selected subjects are incorporated in this report. An evaluation of each bibliography with recommendations for acute and chronic studies are also included.