



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

24 APR 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Review of the Health Risk Assessment of Aerial
Application of Malathion-Bait submitted by California
Department of Health Services

FROM: Penelope A. Fenner-Crisp, Ph.D., Director
Health Effects Division (H7509C) 4/24/91

TO: Anne E. Lindsay, Director
Registration Division (H7505C)

The California Department of Health Services' (CDHS) document "Health Risk Assessment of Aerial Application of Malathion-Bait" has been reviewed by the Health Effects Division's (HED) scientists. In general, HED agrees with CDHS' overall conclusion that a database adequate to support the continued registration of a pesticide for agricultural use may not necessarily be sufficient to support the same pesticide in a more widespread use; in this case, the evaluation of the use of malathion over a large human population (as in urban areas) would require a more extensive database than that which is currently available, given the need to suitably evaluate the exposure and to assure the protection of the general population. Furthermore, CDHS recommends that aerial application of malathion in urban areas be reconsidered in light of the results of the health risk assessment.

HED has the following specific comments on the toxicology and the exposure components of CDHS' risk assessment conclusions:

- (1) There were no actual human monitoring data with respect to post-application exposure. To estimate potential exposure, CDFA used models based on atmospheric concentration measurements (for inhalation dose) and mass deposition data (for oral and dermal dose). CDHS' risk assessment concludes that, under certain high exposure scenarios, there was little or no margin of exposure (margin of safety, as used in the document) for skin irritation and 20% inhibition of acetylcholinesterase activity. Based on these results some population subgroups such as children, the aged, individuals with certain pre-existing diseases and the homeless may be at risk of exhibiting some adverse health effects.



CDHS' margin of exposure estimates were based on model-derived exposure levels and on CDHS' reference exposure levels (REL), which closely approximates the concept of the Agency Reference Dose (RfD) should an RfD be established for each toxicological endpoint. Although these estimates may provide a fair characterization of the risk because of conservative exposure estimates, this characterization still abounds with uncertainties. However, HED is not able to use the available information to derive better exposure estimates or risk estimates for these or any other toxicological endpoints, and the information, as such, would not be considered acceptable to support the registered use of aerial application of the malathion-bait.

- (2) Because of the lack of adequate evidence of carcinogenicity, CDHS does not classify malathion or malaoxon as a carcinogen. However, CDHS does state that there is equivocal evidence of a carcinogenic effect for malaoxon in male and female rats and that these compounds exhibit evidence of genetic toxicity in a variety of in vitro and in vivo assays; therefore, additional chronic studies on these compounds are needed to research the endocrine pathology and the mechanism of the genotoxicity.

HED continues to have a concern for the carcinogenic potential of malathion and malaoxon. Malathion has been classified in Group D with respect to carcinogenicity (i.e., not classifiable as to human carcinogenicity) by the HED Peer Review Committee. The data gaps were identified in the Registration Standard for malathion. For the reregistration of malathion, chronic/oncogenicity studies in the rat are required for both malathion and malaoxon, in addition to an oncogenicity study in the mouse for malathion. Whereas CDHS requires at least two positive studies before a chemical is considered carcinogenic, the Agency may determine that a chemical has carcinogenic potential based on one positive study.

- (3) Based on available information on malathion and other organophosphates, HED has concerns for potential damage to the eye from exposure to malathion. Data to address ocular effects are being required for the reregistration of all organophosphates.
- (4) To reduce the number of assumptions required for a risk assessment of the aerial application of the malathion-bait, HED would find it useful to have toxicological information on the end-product, the malathion-bait. At a minimum, data from an acute testing battery should be available for a health assessment.

Also, to reduce the number of assumptions for a risk assessment, additional exposure data would be useful. HED is currently developing data requirements to address this difficult, and generic, issue of bystander exposure.

- (5) HED's most current DRES analysis based on anticipated residue and crop treatment data shows that exposure from consumption of treated crops is estimated to be approximately 120% of the RfD. For non-nursing infants and children up through age twelve, the dietary exposure ranges between 175% and 250% of the RfD.

Attachments:

OREB memo
TB-I memo
DRES analysis

cc: A. Abramson
K. Baetcke
A. Barton
W. Burnam
R. Engler
A. Jennings
J. Kariya
C. Trichilo



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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APR 18 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: "Exposure Estimation" in: California Department of
Health Services' "Health Risk Assessment of Aerial
Application of Malathion-Bait"

TO: Penelope Fenner-Crisp, Ph.D., Director
Health Effects Division (H7509C)

FROM: Mark I. Dow, Ph.D. *Mark I. Dow*
Special Review and Registration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

THRU: Curt Lunchick, Section Head *Curt Lunchick*
Special Review and Registration Section
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

Charles L. Trichilo, Ph.D., Chief *Charles L. Trichilo*
Occupational and Residential Exposure Branch
Health Effects Division (H7509C)

I have reviewed "Exposure Estimation" pp 7-1 through 7-68 of the document "Health Risk Assessment of Aerial Application of Malathion-Bait" (prepared by S.A. Book, R.J. Jackson, A.M. Fan, and M.J. Bartolomeis for the California Department of Health Services, Feb. 1991). The purpose of the review was to determine the extent of, or the existence of, any human monitoring data resulting from the aerial application of malathion-bait. There are no human monitoring data in the document relative to post-application exposure. The DHS and CDFA collected additional monitoring data during the summer of 1990, however, those data were not available for incorporation in the current risk assessment. Further, the data were not characterized as to whether they were human monitoring data or otherwise.

The monitoring that was performed utilized one square foot pieces of laboratory bench top paper ("Kimbie cards") that were affixed to cardboard and in turn fastened to bricks one foot above the ground. The process measures Mass Deposition which is the "primary method used by CDFA to evaluate the application program." The exposure assessment "uses CDFA mass deposition data collected in February 1990...." The CDFA monitored air at

18 indoor and 19 outdoor sites. Specifications for the air monitors were not presented. "It should be noted that it is uncertain what fraction of inspirable particles were collected" since the "air samplers used by CDFA were not calibrated for particle size collection efficiency...."

Estimates of total acute and subchronic exposure were derived from estimates of inhalation and several routes of oral and dermal exposure. The estimates were based on 11 applications because that was the greatest number of applications in any one area. Quite a number of assumptions were utilized regarding such things as compound half life, rate of decay, plant concentrations, water concentrations, air concentrations, amounts of vegetation and soil and water ingested, and various physical activities that might result in dermal exposure. "Inhalation dose estimates are based on atmospheric concentrations measured both indoors and outdoors. Ingestion and dermal dose estimates are based on malathion and malaoxon mass deposition data on the ground and other upward facing outdoor surfaces."

OREB agrees with several statements in the document with regards to the applicability of the information presented. "The level of uncertainty in estimating exposure doses is probably large, but not quantifiable." "Several assumptions used in the dose estimate calculations are sources of uncertainty. The environmental monitoring was not designed to be 'representative' nor was it designed to look at specific issues addressed by these calculations." "Models, not sampling results, were used to calculate exposures...."

In conclusion, these remarks are in no way to be construed as disparaging. The difficulties involved with deriving exposure estimates based on less than perfect data are not new or unique. However, if this information had been submitted in support of an application for registration, it would not be acceptable. OREB cannot utilize the information in any way to derive more significant estimates of exposure that might result from the aerial application of malathion bait. Obviously, changes in underlying assumptions could alter calculated results. However, since the assumptions used are already quite conservative, any alterations would only tend to reduce the estimated or perceived risk.

As a point of interest, I refer you to the apparent dichotomy of thought contained in the fifth paragraph of the Preface and the concluding paragraph of the Executive Summary. Dr. K.W. Kizer notes that there is concern for theoretically susceptible groups but states that the current evidence indicates that there have been very, very few malathion associated illnesses or reactions. He further indicates that if the Medfly eradication program posed any significant health risks, he would recommend that it be halted immediately. The Executive Summary is much more conservative and suggests that the entire aerial Medfly program be reconsidered in urban areas.

I'll be happy to answer any questions you may have on this matter.

cc: K. Baetcke
F. Chow ✓
L. Dorsey



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

4-23-91

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: California Health Risk Assessment of Aerial
Application of Malathion-Bait

FROM: Brian Dementi, Ph.D., D.A.B.T. *Brian Dementi 4/19/91*
Review Section III, Toxicology Branch I
Health Effects Division (H7509C)

TO: Flora Chow, Chemical Manager
Reregistration Section
Science Analysis & Coordination Branch
Health Effects Division (H7509C)

THRU: Henry Spencer, Ph.D. *Hugh 4/23/91*
Acting Section Head
Review Section III, Toxicology Branch I
Health Effects Division (H7509C) *KH 4/23/91*

The California Department of Health Services (DHS) has completed and published (February, 1991) a risk assessment for the aerial application of malathion-bait in the control/eradication of the mediterranean fruit fly. The assessment estimated doses of malathion and malaoxon that individuals residing in the spray zone would receive as a consequence of a variety of some 25 exposure scenarios. These doses were compared to a parameter termed the Reference Exposure Level (REL) calculated for several toxicity end points to determine if doses received by individuals posed a threat to human health. The REL is defined in the risk assessment as a NOAEL (NOEL) or LOAEL (LOEL) for a given toxicity end point adjusted (divided) by factors of 10 (in most cases) until the major sources of uncertainty (e.g. inter- and intra-species variations, the use of a LOAEL rather than a NOAEL, experimental design, etc.) in the data base have been considered. An REL is a level of exposure at which no adverse human health effects would be anticipated. Hence, according to the California document, health protection is achieved if the estimated or actual human dose of malathion is below the relevant REL. (p. 8-5)

The following conclusions expressed in this risk assessment are cited here uncritically, contingent upon a thorough review of the document within HED.

The risk assessment concluded that under certain exposure scenarios, dose estimates for malathion were greater than relevant RELS



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by more than 10-fold in the cases of dermal irritation and acetylcholinesterase inhibition of 20% or more. The particular exposure scenarios in question included individuals eating unwashed vegetables grown in the backyard and individuals spending a minimum of four hours per day outdoors wearing only shorts during or following malathion-bait applications. (p. 8-45)

The study employed by DHS for acetylcholinesterase inhibition was the human (male) study by Moeller and Rider (1962). The same study serves as the basis for EPA'S RfD. As derived from this study, the REL for acute exposure is the same as EPA's RfD, namely 0.02 mg/kg (p. 8-21). It is upon this figure that the >10-fold exceedance of the REL has been identified in the risk assessment based upon certain circumstances of exposure. It should be noted that the California risk assessment advises that the REL is based upon a dose which actually resulted in 10% acetylcholinesterase inhibition, but is considered a NOAEL in the sense that 10% inhibition is not viewed as producing clinical symptoms, hence, this is a NOAEL rather than a true NOEL (p. 8-11)

The DHS referenced study cited in calculating the REL for dermal irritation was that of Hayes, et. al. (1960), a study which employed human (male) volunteers. This study, while not present on the HED one-liners, was used by the Food and Drug Administration in licensing a 0.5% malathion topical lotion to treat head lice. (pp. 8-9, 10)

Other toxicity end point RELs which were equalled or exceeded (by factors estimated to be less than 10-fold, or of unknown magnitude) under particular circumstances of exposure include those for genetic toxicity (p. 8-25), behavioral effects (indicated in the risk assessment as not well documented in animals or humans) (p. 8-27), developmental effects (p. 8-28), malaoxon acetylcholinesterase inhibition of 20% or more (p. 8-31) and malaoxon dermal effects. (p. 8-33)

In performing the risk assessment, the Malathion Public Health Effects Advisory Committee (MPHEAC), a group of experts appointed by DHS to evaluate certain toxicity parameters, considered the data bases for carcinogenicity and ocular toxicity and concluded in essence that the findings were not sufficiently definitive to determine that either effect should be used as a toxicity end point in assessing risk based upon the exposure data. As to the question of carcinogenicity, the risk assessment document advises that MPHEAC was unable to reach a consensus on whether to classify malathion as a "C" or "D" carcinogen according to EPA's Cancer Risk Assessment Guidelines, but felt that risks likely would be small. The committee endorsed an additional cancer bioassay as is being required by EPA, plus special studies to resolve questions of endocrine pathology. (pp. 8-3, 4). For purposes of comparison, the EPA carcinogenicity peer review of April 1990 placed malathion in category "D" and required new chronic/oncogenicity studies for malathion and malaoxon in the rat and oncogenicity testing in the mouse. Special study requirements to assess endocrine pathology have not been entertained by HED.

On the question of ocular effects, DHS concluded that evidence is insufficient to classify malathion as causing irreversible or severe eye damage as reported for certain residents of Japan following exposure to "numerous and high levels of organophosphate insecticides." "It is not appropriate, therefore, to derive an REL for ocular effects." (p. 8-11) DHS does however support further testing. An HED Peer Review of organophosphate induced eye effects concluded that combined epidemiologic studies and toxicologic data indicate the potential for organophosphates to produce a wide range of ophthalmologic effects. As a result of the peer review, all organophosphates, including malathion, will undergo required testing for ocular effects.

Tox Branch advises, based upon the organophosphate/ocular effects review, that malathion was one of the principal organophosphate pesticides reportedly used in Japan when the ocular effects were identified and published in the Japanese literature. As described in that literature certainly one mode of application of malathion was via helicopter. To the extent that organophosphate ocular toxicity actually occurred in Japan as identified in that literature, it is not possible to conclude that the effects were limited to any particular organophosphate among those principally in use.

Tox Branch is concerned over a physician reported case of legal blindness in a teenager following malathion-bait spraying last year in the Los Angeles California area.

Important quotations after the nature of conclusions appearing in the California risk assessment document might be cited as follows:

"Although the existing database may be adequate to support the continued registration of malathion for use in agriculture to control pests, the data do not necessarily provide information pertinent to the evaluation of the use of this pesticide in urban areas with large populations to control pest infestations." (p. 8-45)

"Based on these results, DHS believes that a subpopulation of potentially sensitive individuals such as children, the aged, individuals with certain pre-existing diseases, and the homeless who receive upper-bound exposures (and in some cases average exposures) to malathion may be at risk of exhibiting some adverse health effects from aerial malathion-bait application." (p. 1-6)

"Given the findings of this risk assessment, DHS recommends that the use of aerial malathion-bait applications in urban areas for agricultural pest eradication be reconsidered. This recommendation excludes the use of malathion in human infectious disease vector control in which the risks of contracting a debilitating or fatal disease are far greater than the potential risks for adverse health effects associated with malathion exposure. Although the theoretical adverse health risks from exposure to aerially applied malathion-bait in the general population may be reduced by following some simple precautions, potential exposures in more sensitive subpopulations may not be avoided

as easily. DHS recognizes the public concerns related to the aerial application of pesticides such as malathion, and the public demand for the development and use of pest control methods that are less intrusive and alarming. Therefore, DHS also recommends that CDFA develop, and when possible, utilize available non-pesticide or selective pesticide (e.g., natural attractants) alternatives to aerial application of pesticides." (p. 8-46)

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

DATE: 04/09/91

PAGE: 1

CHEMICAL INFORMATION		STUDY TYPE		EFFECTS		REFERENCE DOSES		DATA GAPS/COMMENTS		STATUS	
Malathion Caswell #535 CAS No. 121-75-5 A.I. CODE: 057701 CFR No. 180.111	Human CHE Study NOEL= 0.2300 mg/kg 0.00 ppm LEL= 0.3400 mg/kg 0.00 ppm ONCO: Class D (HED NOTE).			Decreased CHE activity.		PAD1 UF -->10 OPP RfD= 0.020000 EPA RfD= 0.020000		Chronic feeding- dog Reproduction- rat Developmental tox- rat Developmental tox- rabbit		HED complete 08/29/86. HED reassess 03/06/87. EPA verified 03/18/87. WHO last reviewed 1966. On IRIS.	
				No evidence of oncogeni- city in rats, mouse study equivocal.							

TOTAL THRC (MG/KG BODY WEIGHT/DAY)

POPULATION SUBGROUP

POPULATION SUBGROUP	CURRENT THRC*		NEW THRC**		NEW THRC AS PERCENT OF RFD		DIFFERENCE AS PERCENT OF RFD		EFFECT OF ANTICIPATED RESIDUES ARC		XRFD	
U.S. POPULATION - 48 STATES	0.099939	0.099939	0.099939	499.693590	0.000000	0.000000	0.000000	0.000000	0.024216	121.07896		
U.S. POPULATION - SPRING SEASON	0.096943	0.096943	0.096943	484.715890	0.000000	0.000000	0.000000	0.000000	0.023980	119.90088		
U.S. POPULATION - SUMMER SEASON	0.100728	0.100728	0.100728	503.640215	0.000000	0.000000	0.000000	0.000000	0.024313	121.56351		
U.S. POPULATION - FALL SEASON	0.100668	0.100668	0.100668	503.341430	0.000000	0.000000	0.000000	0.000000	0.024223	121.11663		
U.S. POPULATION - WINTER SEASON	0.100411	0.100411	0.100411	502.052500	0.000000	0.000000	0.000000	0.000000	0.024094	120.46755		
NORTHEAST REGION	0.106758	0.106758	0.106758	533.792385	0.000000	0.000000	0.000000	0.000000	0.025018	125.08849		
NORTH CENTRAL REGION	0.099001	0.099001	0.099001	495.004630	0.000000	0.000000	0.000000	0.000000	0.024329	121.64577		
SOUTHERN REGION	0.091933	0.091933	0.091933	459.663725	0.000000	0.000000	0.000000	0.000000	0.023089	115.44658		
WESTERN REGION	0.104591	0.104591	0.104591	522.956545	0.000000	0.000000	0.000000	0.000000	0.024569	122.84724		
HISPANICS	0.115940	0.115940	0.115940	579.698390	0.000000	0.000000	0.000000	0.000000	0.026948	134.74178		
NON-HISPANIC WHITES	0.098960	0.098960	0.098960	494.799880	0.000000	0.000000	0.000000	0.000000	0.023984	119.92179		
NON-HISPANIC BLACKS	0.094905	0.094905	0.094905	474.525365	0.000000	0.000000	0.000000	0.000000	0.023571	117.85286		
NON-HISPANIC OTHERS	0.115359	0.115359	0.115359	576.795165	0.000000	0.000000	0.000000	0.000000	0.027195	135.97268		
NURSING INFANTS (< 1 YEAR OLD)	0.139474	0.139474	0.139474	697.371820	0.000000	0.000000	0.000000	0.000000	0.017960	89.79827		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.262863	0.262863	0.262863	1314.317310	0.000000	0.000000	0.000000	0.000000	0.038455	192.27304		
FEMALES (13+ YEARS, PREGNANT)	0.074800	0.074800	0.074800	373.999955	0.000000	0.000000	0.000000	0.000000	0.017283	86.41316		
FEMALES 13+ YEARS, NURSING	0.083441	0.083441	0.083441	417.202605	0.000000	0.000000	0.000000	0.000000	0.018827	94.13492		
CHILDREN (1-6 YEARS OLD)	0.222584	0.222584	0.222584	1112.920045	0.000000	0.000000	0.000000	0.000000	0.049740	248.70121		
CHILDREN (7-12 YEARS OLD)	0.145287	0.145287	0.145287	726.433185	0.000000	0.000000	0.000000	0.000000	0.035075	175.37628		
MALES (13-19 YEARS OLD)	0.093911	0.093911	0.093911	469.555440	0.000000	0.000000	0.000000	0.000000	0.025050	125.24784		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.081845	0.081845	0.081845	409.223310	0.000000	0.000000	0.000000	0.000000	0.020532	102.65956		
MALES (20 YEARS AND OLDER)	0.074530	0.074530	0.074530	372.651095	0.000000	0.000000	0.000000	0.000000	0.020313	101.56389		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.073172	0.073172	0.073172	365.860700	0.000000	0.000000	0.000000	0.000000	0.017574	87.87244		

*Current THRC does not include new or pending tolerances.

**New THRC includes new, pending, and published tolerances.



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

AUG 8 1990

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: California Malathion Section 18 Amendment - Incremental Occupational and Residential Exposure and Risk
(HED # ~~Intra~~ 0073)

FROM: Michael P. Firestone, Ph.D., Supervisory Chemist
Non-Dietary Exposure Branch/HED (H7509C)

THRU: Charles L. Trichilo, Ph.D., Chief
Non-Dietary Exposure Branch/HED (H7509C)

TO: Reto Engler, Chief
Science Analysis and Coordination Branch/HED (H7509C)

X Deferral to SACB and/or TOX-I

The purpose of this memorandum is to evaluate the incremental human non-dietary exposure and risk resulting from the current (April 17, 1990) amendment to the 1989-issued Section 18 quarantine exemption covering the control of fruit fly members of the family Tephritidae in California.

It appears that the purpose of the April 17, 1990 amendment prepared by the California Department of Food and Agriculture (CDFA) was to broaden the "Crop/Site/Commodity" section of the Section 18 quarantine exemption to include the wording "Commercial and residential plantings of food and feed crops such as but not limited to ..." CDFA claims that this language is "comparable to the standard wording used on other Section 18 quarantine exemptions."

According to CDFA, this amendment was prepared to include "any additional crops or plantings which may be encountered ... because the quarantine area is constantly changing with the discovery of new medfly infestations." As such, it appears that the current amendment has been submitted to cover food contamination concerns associated with the Federal Food, Drug and Cosmetic Act (FFDCA) and is not specifically designed to increase the number of acres treated or the amount of malathion applied in conjunction with the 1989 Section 18 quarantine program.

Thus, NDEB concludes based on the information available to date that the subject April 17, 1990 amendment will result in negligible incremental human non-dietary exposure or risk.

It should be noted that NDEB does not currently have data available to assess residential post-application (including bystander) exposure as a result of the California Section 18 program or similar ones in other States. In order to support the development of a quantitative risk assessment, exposure data reflecting air and ground surface residue monitoring following repeated treatments and residue dissipation with time would be required. The exposure data currently being generated by CDFA may partially fulfill this need.

NDEB defers to SACB and/or TOX-I as to the need for a quantitative risk assessment and the endpoint(s) of possible regulatory concern such as cholinesterase depression, eye effects, carcinogenicity, etc. The endpoint(s) of concern could affect the nature of the exposure data required.

cc: Larry Dorsey/SACB
Karl Baetcke/TOX-I
Curt Lunchick/NDEB
Circulation
Correspondence File
Malathion File
Becky Cool/RD (H7505C)