CASWELL FILE
8-22-90

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

AUG 22 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Naled (Dibrom-14) - Potential 6(a)(2) Data
ID Nos. 16-819/16-830

Chemical (Caswell) No.: 586
RD Record No.: 265,827/267,938
HED Project No.: 0-1668

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

TO: William Miller/Dan Peacock, PM Team 16
Insecticide-Rodenticide Branch
Registration Division (H7505C)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

Registrant: Chevron Chemical Company, Richmond, CA (represented by Valent U.S.A., Walnut Creek, CA)

Request

By memorandum of July 30, 1990, RD's PM 16 asks HED's TB-I to appraise two separate communications reporting adverse effects from:

1. The (presumably unintentional) exposure of a New York State adolescent (and as well, comment on proper usage/practice/precautions for naled application); and

2. A preliminary report of a delayed neurotoxicity study recently commissioned in England on "Technical Naled."

Details of the Requests

1. Apparent Adverse Effects of Human Exposure

The first request asks us to comment upon a submission made to OPP 3 years ago (by letter to D. Campt dated October 23, 1987) by [redacted] of Lake Placid, NY, asserting that his 17-year-old son was severely affected ("headache, shortness of breath, stomach upset") during (or following?) aerial spraying of the town with Dibrom-14 for control of black flies and mosquitoes. Further, it was asserted that Dibrom was found in a blood sample from the boy, with accompanying support for this exposure in the form of a cover letter from Dr. William J. Rea, Dallas, TX, with a laboratory report from Enviro-Health Labs, Richardson, TX, which listed the following values for the indicated compounds presumably present in a sample of the boy's blood collected August 6, 1987 and analyzed on August 12, 1987:

Compound	Results ng/mL (ppb)
Methyl Bromide	< 5.0
Vinyl Bromide	< 1.0
Ethyl Bromide	< 1.0
Bromochloromethane	< 1.0
1-Bromo-2-chloroethane	< 1.0
Dibromomethane	10.7
Bromodichloromethane	5.1
1-Bromo-1-chloroethane	< 1.0
Dibromomethylenes (cis & trans)	< 1.0
Chlorodibromoethane	< 1.0
1,2-dibromethane (EDB)	< 1.0
Bromoform	< 1.0
Bromobenzene	< 1.0
Dibromochloropropane (DBCP)	37.7
n-Pentane	28.0
2,2-Dimethylbutane	< 1.0
Cyclopentane	< 1.0
2-Methyl pentane	< 1.0
3-Methyl pentane	11.0
n-Hexane	7.4
n-Heptane	< 2.0

PRIVACY ACT INFORMATION IS NOT INCLUDED

Dr. Rea was of the opinion that "The Dibrom-14 in [redacted] blood probably came from the spraying."

Finally, this package contained a copy of a letter (dated May 10, 1984) to the father from the same Dallas medical group (Dr. Rea and associates), which reported that the son had been under their (continuous?) medical care during the period September 16 to October 7, 1982, for "immunoglobulin G-deficiency, chest wall syndrome, rhinitis, atopic disease, hyper gamma E immunoglobulin syndrome, 'cephalgia' (sic!*), food and chemical sensitivities, especially to "natural gas" (sic!**)

Because of the patient's sensitivities, this medical group warned against exposure to even trace amounts of ambient ("airborne") residues of "common waxes, cleaners, pesticides, and other compounds," since this can result in "severe aggravation of the illness."

Perhaps as a consequence of seeking TB's appraisal of this incidence report, RD requests our opinion whether: (1) we (EPA) should ask for data additional to those required by the current DCI that Reregistration is developing; and (2) the Agency should expand the Farm Worker Protection Regulations to include persons sprayed during mosquito control programs.

2. Adverse Effects in a Delayed Neurotoxicity Study

Under cover of July 11, 1990, Valent U.S.A. (agent for Chevron) submitted a preliminary report of adverse effects encountered during the course of a delayed neurotoxicity study in Leghorn hens treated orally with naled technical, conducted at Huntingdon Research Centre (HRC), Cambridgeshire (UK).

As reported in the cover letter (and evident in the unaudited drafts of neuropathological grading of individual birds in appended tabulations), there appeared to be a slight but statistically significant increase over control (both in incidence and severity) in axonal degeneration of spinal cords among naled-treated birds treated with naled at the LD_{50} (42 mg/kg), as well as a nonsignificant increased degeneration in peripheral nerve tissue.

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*The accepted medical term for headache is cephalalgia.
**Probably unique among the world's population.

The investigators have interpreted this effect as "equivocal," since these histopathological findings did not correspond to any observed clinical effects in the treated birds (e.g., no locomotor ataxia), and as well there was no depression of spinal cord neurotoxic esterase (although brain cholinesterase was reduced).

TB Appraisals

1. The Adverse Incidence Report

TB did receive prior notification of this subject incidence report shortly after submission to the Agency, but made no specific comment or response at that time, other than noting it for the naled file (Memorandum: Hauswirth to Miller/Peacock, stamp-dated May 5, 1988; Tox. Proj. 8-0607).

In response to the current resubmission, the Agency sympathizes with the plight of this young man, apparently afflicted with such grave immunological defects* (perhaps inherited) as to have made him exquisitely susceptible to a great many elements of his environment. Had young [redacted] indeed been exposed (inadvertently perhaps) to aerially-sprayed Dibrom-14, he certainly might have reacted almost immediately with the typical syndrome of organophosphate-type effects common to this class of insecticide, and/or to any one or other component of the product (which, in the concentrate form, contains 85% of the active ingredient, naled, plus 15% inerts--in the form of light petroleum distillates, mainly [redacted] However, there does not appear to be any definitive clinical or biochemical evidence submitted of Dibrom-14 exposure, or accumulation, certainly not based on the assertion of the Dallas lab claiming to find "Dibrom-14 in [redacted] blood." The lab report listed six chemicals assayed from this single blood sample** present in excess of the limits of sensitivity of methods, or population average, to support the indictment, but none of these are present in any naled formulations as contaminants, impurities, derivatives, or metabolites (see Confidential Statements of Formula and

PRIVACY ACT INFORMATION IS NOT INCLUDED

*As diagnosed by the Texas medical facility where he spent some time in 1984.

**Dibromethane, bromdichlormethane, dibromochloropropane (DBCP), n-pentane, 3-methyl pentane, n-hexane.

metabolic scheme appended). [None of these were apparently analyzed for; if [redacted]out was really a consequence of naled exposure, surely dichlorvos (DDVP), a principal metabolite, should have been found, as well as measurable quantities of methyl bromide (actually analyzed for, but not found) and bromodichloroacetaldehyde.]

In response to the PM's concerns about label lapse for mosquito control,* we have on file available (and acceptable) toxicity data on both the technical and formulated products, and do not require, at present, any additional data other than those currently proposed by SRRD** (see appended memorandum: Mauer to Lowry, dated February 13, 1990).

Finally, the proposed guidelines concerning Farm Worker Protection Regulations (40 CFR 156/170 - see FEDERAL REGISTER Vol. 53, No. 131, Friday, July 8, 1988, pages 25970-26021) are currently being revised toward a final rule, but we are told will not include any changes in consideration for persons sprayed during mosquito control programs [cf: Dr. Patricia Breslin, Chief, Occupational Safety Branch/FOD (H7506C)]. We are further informed that, to avoid such incidences, it is the responsibility of the State (in this case, New York State) to register super-sensitive individuals, as well as to announce impending spraying for such purposes for their protection (e.g., through the State's Pesticide Bureau of their Departments of Agriculture and/or Environment; or Department of Health; or local authorities, sig., The Adirondack Park Agency; or failing all else, the Governor's office).

2. Delayed Neurotoxicity Study (Putative Adverse Effect - 6(a)(2) Data)

This submission is a preliminary report (consisting of only an unaudited draft of data), suggesting histopathological evidence for delayed neurotoxicity

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*Where inadvertent spraying of bystanders is apparently not precluded by current naled labels, since applicators need not observe the standard 24-hour reentry prohibition as mandated for crop use.

**85-1 - General Metabolism in the Rat; 85-2 - Dermal Penetration.

(but in the apparent absence of any clinical or biochemical correlation). We await submission of the lab's full (Final) report before we can evaluate this study.

The cover reported that Naled Technical (Chevron Dibrom Technical, Lot No. SX820) was previously tested over 10 years ago for neurotoxicity in hens* treated up to the oral LD_{50} level (= 110 mg/kg), with no apparent effects on behavior, body weight and food consumption, neurologic scores, or gross or histological parameters of spinal cords (Memorandum: Dykstra to M. Mautz, PM 16, dated January 17, 1979; Document No. 007428). The Agency judged this study CORE-MINIMUM data, affirming the lab's conclusion that this lot of Dibrom Technical was not a delayed neurotoxic agent.

Attachments

*The Evaluation of Dibrom as a Potential Neurotoxic Agent Following Oral Administration to Hens Protected by Atropine Sulfate, performed by Food/Drug Research Laboratories (FDRL) No. 598, November 14, 1978) Accession No. 236682 (EPA Registration No. 239-1633).

ATTACHMENT I

(Naled - Proposed Data Call-In Notice)

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

MEMORANDUM FEB 12 990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: NALED --- Proposed DCI

EPA ID# 239-1633

Chemical (Caswell) 586
RD Record No. 258,363
HED Project 0-0543

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I (IRS)
Health Effects Division (H7509C)

2-6-90

TO: Brigid Lowry, PM 74
Special Review & Reregistration Division (H7508C)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I (IRS)
Health Effects Division (H7509C)

2/11/90

Request: SRRD requests confirmation of the following outstanding tox. data requirements, in order to fully evaluate the risk of exposure to dichlorvos (DDVP, the main putative metabolite of both naled and trichlorfon). In addition, SRRD asks TB to list any additional data requirements for naled.

SRRD List of Data Requirements:

85-1 General metabolism in the rat, to characterize metabolites.

85-2 Dermal penetration (if shown to metabolize to DDVP in mammals).

TB Conclusions: The two tox studies listed above represent data still required for naled; no other data gaps exist at this time.

ATTACHMENT II

1. Composition of Technical Naled (Generic).

2. Chevron Naled Technical (Alternate Formulation; AMVAC, EPA Registration No. 239-1633).

3. Chevron Dibrom-14 Concentrate (Chevron, EPA Registration No. 239-1721).

4. Metabolism of Naled (adapted)

RIN 3201-96

NALED REVIEW

Page _____ is not included in this copy.

Pages 10 through 12 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

✓ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

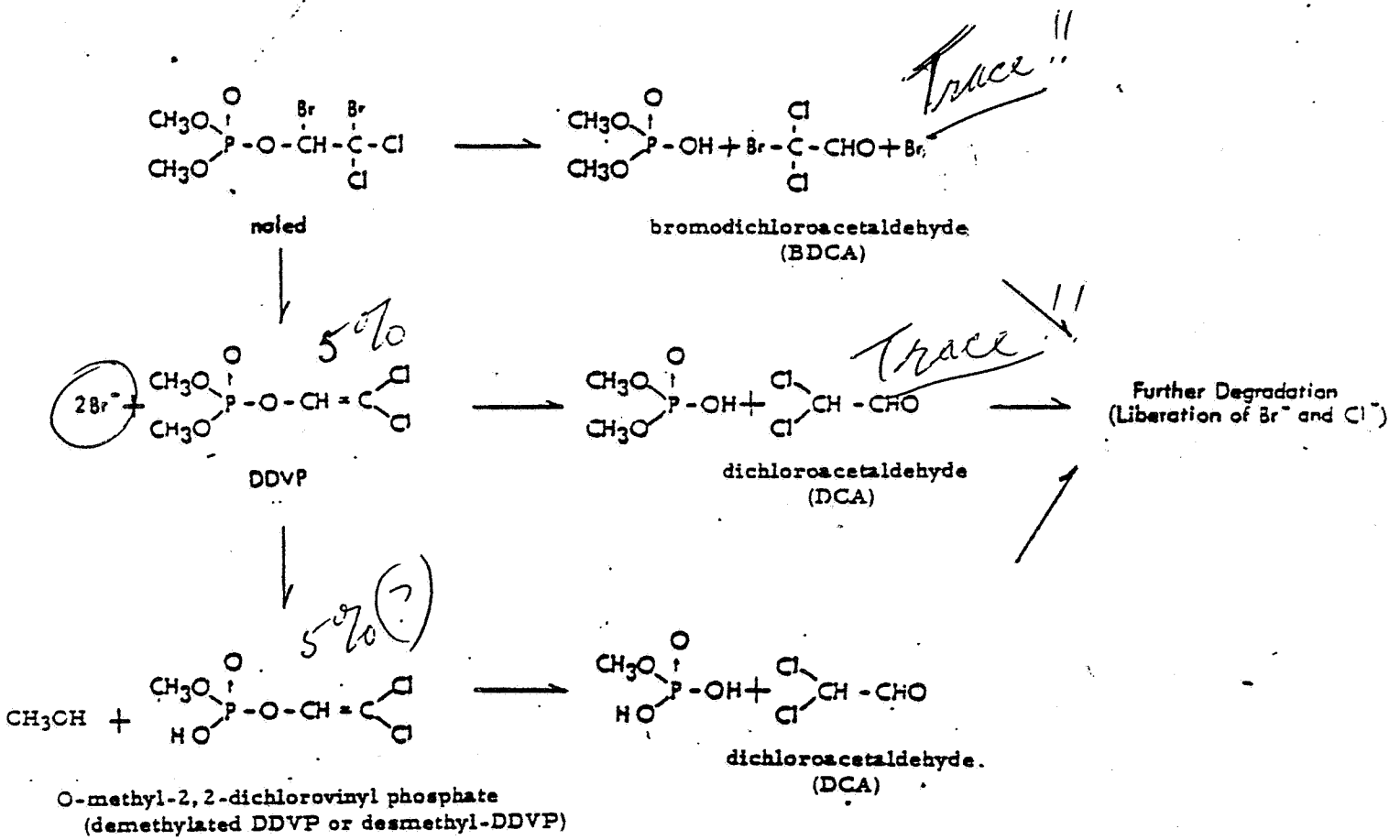
The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

METABOLIC SCHEME FOR NALED
(Plants/Farm Animals)

CONFIDENTIAL

FIGURE I

METABOLISM OF NALED



Adapted from: Chevron Chemical Co., 1966, MRID 00074647, and
Menzie, C.M., 1969; Metabolism of Pesticides, U.S. Department of the Interior, Washington, D.C.

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