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ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

[OPP-30000/57; FRL _____]

2,4-D, 2,4-DB, and 2,4-DP; PROPOSED DECISION NOT TO INITIATE A SPECIAL REVIEW

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice; Proposed Decision Not To Initiate a Special Review.

SUMMARY: This document announces EPA's proposed decision not to initiate a Special Review of 2,4-D, 2,4-DB, and 2,4-DP based on carcinogenicity. The Agency's decision is based on a consensus of opinion from EPA scientists, national experts on epidemiology, and the FIFRA Scientific Advisory Panel, that existing epidemiologic data are inadequate to assess the carcinogenic potential of 2,4-D. In addition, the Agency has concluded that existing laboratory data provide insufficient evidence of carcinogenicity. Therefore, EPA has determined that a Special Review is not appropriate at this time.

DATE: Comments on this Notice must be received by [insert date 60 days after date of publication in the FEDERAL REGISTER].

ADDRESS: Submit three sets of written comments, bearing the document control number [OPP-30000/57] by mail to:

Information Services Branch,
Program Management and Support Division (TS-767C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St., SW,
Washington, DC 20460.

87P-1674

In person, bring comments to:

Rm. 236, Crystal Mall #2,

1921 Jefferson Davis Highway,

Arlington, VA.

Information submitted in any comment concerning this Notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR Part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public docket. Information not marked confidential may be disclosed publicly by EPA without prior notice to the submitter. The 2,4-D public docket, which contains all non-CBI written comments and the corresponding index will be available for public inspection in Rm. 236 at the Virginia address given above from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays.

FOR FURTHER INFORMATION CONTACT: By mail:

W. Michael McDavit,

Special Review Branch,

Registration Division (TS-767C),

Office of Pesticide Programs,

Environmental Protection Agency,

401 M St., SW,

Washington, DC 20460.

Office location and telephone number:

Rm. 1006, Crystal Mall #2,

1921 Jefferson Davis Highway,
Arlington, VA,
(703-557-1787).

SUPPLEMENTARY INFORMATION: This Notice announces EPA's proposed decision not to initiate a Special Review of 2,4-dichlorophenoxyacetic (2,4-D), 2-(2,4-dichlorophenoxy) butyric acid (2,4-DB), and 2-(2,4-dichlorophenoxy) propionic acid (2,4-DP), and sets forth the rationale for that proposed decision. In summary, EPA has re-evaluated the concerns raised in the September 22, 1986, and December 3, 1986, preliminary notifications to registrants and applicants in light of other relevant information that, in part, has become available since issuance of the preliminary notifications. Based on this review, EPA has determined that a Special Review of 2,4-D, 2,4-DB, 2,4-DP is not warranted at this time.

I. INTRODUCTION

A. REGULATORY BACKGROUND

The common name for the herbicide 2,4-dichlorophenoxyacetic acid is 2,4-D. The herbicides 2,4-DB or 2-(2,4-dichlorophenoxy) butyric acid and 2,4-DP or 2-(2,4-dichlorophenoxy) propionic acid are structural analogs of 2,4-D. Including the various derivatives of these three chemicals (esters and salts), over 1500 registered pesticide products contain 2,4-D, 2,4-DB, or 2,4-DP as active ingredients.

The active ingredient 2,4-D, first registered in 1948, is a popular, systemic herbicide widely used for controlling broadleaf weeds on a large number of food and non-food crops.

It is also used as a growth regulator on citrus. The majority of 2,4-D is used to control weeds in wheat, field corn, grain sorghum, sugar cane, rice, barley, and range and pastureland. In addition, 2,4-D is used for aquatic weed and forest management, as well as weed control around the home.

The herbicide 2,4-DB is a selective, systemic herbicide used for postemergence weed control. The majority of 2,4-DB is used to control broadleaf weeds in soybeans, alfalfa, and peanuts.

The herbicide 2,4-DP is a selective, systemic herbicide used to control broadleaf weeds, annual grasses, and woody plants. The majority of 2,4-DP is used to control pest plants in turf (ornamental, golf course and lawn areas), non-bearing citrus fruit, rights-of-way (utility, railroads, highways, etc.), and forestry.

On August 28, 1980, after reviewing all available health effects information on 2,4-D and consulting with the Scientific Advisory Panel (SAP), the Agency issued a Data Call-In notice (DCI) pursuant to section 3(c)(2)(B) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) to the registrants of 2,4-D. This notice required registrants to submit studies on the following areas: acute toxicity, oncogenicity in the rat and mouse, reproductive effects, teratogenicity (birth defects), neurotoxicity, and metabolism. Since that time, all of these required data have been received and reviewed by the Agency.

The Agency has also recently reviewed a number of epidemiology studies relevant to these pesticides, including

a new study conducted by the National Cancer Institute and University of Kansas that found an association between farm herbicide use and non-Hodgkin's lymphoma. Published in the Journal of the American Medical Association on September 5, 1986, the authors of this study concluded that the use of phenoxy herbicides, including 2,4-D, was linked to an increased cancer risk among farmers handling such herbicides.

Based on this epidemiological evidence, on September 22, 1986, the Agency issued a preliminary notification of Special Review to the registrants of 2,4-D pursuant to 40 CFR 154.21. On December 3, 1986, the Agency issued a similar preliminary notification of Special Review to the registrants of 2,4-DB and 2,4-DP because the Agency believed that these compounds were toxicologically similar to 2,4-D and should be reviewed at the same time.

B. LEGAL BACKGROUND

A pesticide product may be sold or distributed in the United States only if it is registered or exempt from registration under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as amended (7 U.S.C. 136 et seq.). Before a product can be registered it must be shown that it can be used without causing "unreasonable adverse effects on the environment", [FIFRA section 3(c)(5)]. The term "unreasonable adverse effects on the environment" is defined in FIFRA section 2(bb) as "any unreasonable risk to man or the environment, taking into account the economic, social,

and environmental costs and benefits of the use of any pesticide." The burden of proving that a pesticide meets this standard for registration is, at all times, on the proponent of initial or continued registration. If at any time the Agency determines that a pesticide no longer meets this standard, the Administrator may cancel this registration under section 6 of FIFRA.

The Special Review process provides a mechanism to permit public participation in EPA's deliberations prior to issuance of any Notice of Final Determination describing the regulatory action which the Administrator has selected. The Special Review process, which was previously called the Rebuttable Presumption Against Registration (RPAR) process, is described in 40 CFR Part 154, published in the FEDERAL REGISTER of November 25, 1985 (50 FR 49015).

Prior to formal initiation of a Special Review, a preliminary notification is sent to registrants and applicants for registration pursuant to 40 CFR 154.21 announcing that the Agency is considering commencing a Special Review. In this case, that notification was issued on September 22, 1986 for 2,4-D, and on December 3, 1986 for 2,4-DB and 2,4-DP. Registrants and applicants for registration were given 30 days to comment on the Agency's proposal to commence a Special Review. Most registrants responded to the notifications by concurring on one particular comment provided in response to the September 22, 1986, 2,4-D notification on behalf of the Industry Task Force on 2,4-D Research Data. A few unique comments

were also received in response to the December 3, 1986 notification. These comments will be briefly addressed in Unit IV of this Notice.

If the Agency determines, after issuance of a notification pursuant to 40 CFR 154.21, that it will not conduct a Special Review, it is required under 40 CFR 154.23 to issue a proposed decision to be published in the FEDERAL REGISTER. This Notice is being issued under 40 CFR 154.23. That regulation requires that a period of not less than 30 days be provided for public comment on the Proposed Decision Not To Initiate a Special Review. Subsequent to receipt and evaluation of comments on the Proposed Decision Not To Initiate a Special Review, the Administrator is required by 40 CFR 154.25 to publish in the FEDERAL REGISTER his final decision regarding whether or not a Special Review will be conducted.

II. RISK CONCERNS UNDERLYING 40 CFR 154.21 NOTIFICATION

A. EPIDEMIOLOGIC EVIDENCE

The preliminary notifications under 40 CFR 154.21 were issued as a result of Agency concerns raised by the findings of a new epidemiological study of Kansas farmers. The researchers had found an association between farm herbicide use and non-Hodgkin's lymphomas in farmers based on a population-based case control study (Vol. 25, No. 9, Journal of the American Medical Association, pp. 1141-1147) conducted by the National Cancer Institute and the University of Kansas.

This study was performed to determine if there was any relationship between agricultural herbicide use and soft-tissue sarcoma, Hodgkin's disease, or non-Hodgkin's lymphoma. Newly diagnosed cases of the three diseases were taken from a population-based registry covering the State of Kansas and compared with control groups from the general population of Kansas using Medicare and mortality files. Telephone interviews were then conducted with living individuals (or next-of-kin for deceased individuals) belonging to case and control groups. Numerous questions were asked with respect to farming practices and the use of pesticides. An attempt was made to corroborate information from telephone interviews with records or knowledge of pesticide use by local suppliers of pesticides.

In summary, the study found that Kansas farmers who used certain types of herbicides had an excess risk for developing non-Hodgkin's lymphoma. No association was found between farm herbicide use and soft-tissue sarcoma and Hodgkin's disease. Farmers exposed to the herbicides for more than 20 days each year had six times the risk of developing non-Hodgkin's lymphomas when compared to controls. Among these frequent users, those who mixed or applied the herbicides themselves had eight times the risk. These excess risks were reportedly associated with the use of phenoxyacetic herbicides, including 2,4-D.

EPA scientists and four epidemiology experts, requested by EPA to review the new evidence, generally agreed that the NCI/Kansas study was well conducted and that the study served

as a good basis for a hypothesis of a non-Hodgkin's lymphoma and phenoxy herbicide association. Notwithstanding the lack of specificity for 2,4-D, the study was regarded by the reviewers as the most relevant epidemiological study of its kind that pertains to 2,4-D as a pesticide and provides a sound foundation for further inquiries.

A number of critical problem areas, common to many epidemiology studies, have been noted by reviewers. Some of the key areas of concern are the lack of appropriate controls, exposure to multiple chemicals, and insufficient information on actual exposure to 2,4-D and other pesticides.

In order to evaluate the occurrence of non-Hodgkin's lymphoma cases among farmers with exposure to 2,4-D, appropriate study controls should be used. Farmers have different lifestyles (e.g., diet, exposure to animal viruses) than the general population. Differences in habit and lifestyle may confound results when comparisons are made with controls from the general population. In this case, the study did not choose controls based on occupation and, therefore, it is quite possible that lifestyle factors other than herbicide use may have confounded the results.

Farmers are frequently exposed to other chemicals or potentially tumorigenic agents which could account for some or all of the non-Hodgkin's lymphoma cases. Researchers did report some positive associations with the use of other types of pesticides, such as fungicides and insecticides. In

addition, before the phenoxy herbicide, 2,4,5-T, was suspended by the Agency in 1979 based in part on the risk posed by the presence of the carcinogenic impurity, 2,3,7,8-tetrachloro-dibenzo-p-dioxin, farmers in Kansas used pesticide products containing 2,4,5-T. Fertilizers, fuel, and other environmental toxicants, as well as biological agents (e.g., viruses) may also present some risk of non-Hodgkin's lymphoma for farmers. Unless exposure variables associated with farming are better controlled, it is difficult to reach conclusions on any contribution of 2,4-D or other specific phenoxy herbicides to the onset of non-Hodgkin's lymphoma in farmers.

The information obtained on 2,4-D use and exposure is incomplete. Reported use, particularly when that use occurred many years previously, is not necessarily a good surrogate measure of exposure. This type of information is useful, but substantially less reliable than some quantitative measure of exposure. Information obtained from next-of-kin should be used with caution. Living farmers and next-of-kin frequently have incomplete recall with respect to specific pesticide names or work practices. Although researchers tried to verify the veracity of the information gathered from telephone interviews by contacting a sample of pesticide suppliers, only about half of the contacted suppliers were able to confirm respondents' answers concerning use of 2,4-D (personal communication, Blondell 1987).

Some reviewers noted an apparent underreporting of all herbicide use. U.S. Department of Agriculture records indicate

that significantly more pesticides were used in Kansas than was suggested by the results of the telephone survey. This discrepancy alone introduces substantial uncertainty in the pesticide use information obtained from and relied on in this study.

Taken together, these problem areas or uncertainties make it impossible to pinpoint 2,4-D alone as the causative agent in these particular non-Hodgkin's lymphoma cases. As previously mentioned, uncertainties of these kinds are typically present to some degree in all epidemiology studies. Nonetheless, findings of epidemiology studies are frequently insightful and, on occasion, such insight is sufficient for policy-making and regulation. In this case, the extent and degree of these weaknesses limit the usefulness of the study for regulatory purposes.

A number of other epidemiological studies pertaining to 2,4-D were also evaluated by the Agency. Some of the existing epidemiologic studies on 2,4-D and related compounds indicate an association with cancer in humans and others do not. Those studies finding a relationship with cancer in humans were determined to be inadequate for establishing a specific association between cancer risk and 2,4-D use. As mentioned above, the NCI/Kansas study, while relevant to farmers handling phenoxy herbicides, was also determined to be inadequate for establishing a specific association between 2,4-D and non-Hodgkins lymphoma.

In addition, a recently published epidemiologic study designed to address the same issue as the NCI/Kansas study, that is, the relationship between occupational exposure to phenoxy herbicides and cancer in humans, did not confirm the NCI/Kansas study's conclusions with respect to non-Hodgkins lymphoma. Woods, et al. (Soft Tissue Sarcoma and Non-Hodgkins Lymphoma in Relation to Phenoxyherbicide and Chlorinated Phenol Exposure in Western Washington, Journal of the National Cancer Institute 1987; 78: 899-910) studied male farmers handling a variety of phenoxy herbicides and chlorinated phenols, including 2,4-D, and found "small but significantly increased risks of developing [non-Hodgkins lymphoma] in association with some occupational activities where phenoxyherbicides have been used in combination with other types of chemicals, particularly for prolonged periods." However, the investigators did not find a positive association between increased cancer risks and exposure to 2,4-D.

B. LABORATORY EVIDENCE

In response to the Data Call-In notice issued in 1980, the Industry Task Force on 2,4-D Research Data sponsored, among other things, oncogenicity studies in the rat and mouse. The rat study found equivocal evidence of oncogenicity and the mouse study found no treatment-related oncogenic responses.

In the rat, 2,4-D (97.5 percent purity) was administered in the diet to male and female rats at levels of 0, 1, 5, 15, and 45 mg/kg/day for 24 months. At an interim sacrifice of

53 weeks, an apparent treatment-related increased incidence of brain tumors (astrocytomas) was observed in male animals. No tumor response related to 2,4-D administration was observed in female rats.

The results of the final rat study were subjected to two statistical evaluations. Using the Fisher-Exact test, the increased incidence of tumors seen in male animals at the high dose level was not statistically significant when compared to control male animals. Using the Cochran-Armitage trend test, 2,4-D administration was found to be associated with a marginally statistically significant positive dose-related trend for astrocytomas in male rats. Thus, neither evaluation found strong statistical evidence of oncogenicity in the rat.

In the mouse, 2,4-D (97.5 percent purity) was administered in the diet to male and female animals at levels of 0, 1, 15, and 45 mg/kg/day for 24 months. No oncogenic effects attributable to 2,4-D administration were found in either male or female mice.

Although there were no oncogenic effects observed in either sex of the mouse and only marginally statistical oncogenic effects observed in the male rat, the Agency still does not believe there are adequate laboratory animal data to unequivocally assess the carcinogenic potential of 2,4-D. This is predicated on the Agency's conclusion that a Maximum Tolerated Dose (MTD) was apparently not achieved in either test animal. (A MTD, usually the highest dose tested in an oncogenicity study, is a level slightly below the level which

resulted in significant life-threatening toxicity in a subchronic study. The level should not be selected too far below a life threatening level because the highest dose tested in an oncogenicity study should elicit significant toxicity without substantially altering the normal life-span of the test species from effects other than tumor formation.)

Based on the Agency's most current review of the chronic studies and on the results of subchronic studies with 2,4-D, the highest dose tested (45 mg/kg) in both the rat and mouse oncogenicity studies did not achieve a MTD (45 mg/kg is estimated to be only one-third to one-half of the MTD).

In 1985, scientists from NIH's National Toxicology Program (NTP) questioned the dose levels selected for the oncogenicity studies based on their evaluation of tissue slides taken from the subchronic studies and an interim sacrifice of test animals in both two year oncogenicity studies. The NTP pathologists concluded unanimously that the various kidney lesions observed in the subchronic studies, which were used to estimate the MTD and to support the dose levels used in the oncogenicity studies, were minimal in severity and clearly not life-threatening even at the highest dose of 150 mg/kg. They also concluded that the interim sacrifice data from the oncogenicity studies showed only minimal toxicity at the highest dose

tested (45 mg/kg). Their overall conclusion was that the oncogenicity studies on 2,4-D were probably not being conducted at a MTD.

Having now evaluated the two year oncogenicity studies and having considered the scientific opinion of the NTP scientists, the Agency has decided to require, under authority of FIFRA section 3(c)(2)(B), additional oncogenicity testing in the rat and mouse to ensure that a MTD is achieved.

Additional toxicological information, including more detailed reviews of the rat and mouse studies, is available in the 2,4-D public docket.

In April 1987 the Agency concluded that the rat evidence provided limited evidence of oncogenicity in animals. Furthermore, the Agency concluded that although the NCI/Kansas study was well conducted, it provided "inadequate" evidence of cancer in humans attributable specifically to 2,4-D. Given these two conclusions, the Agency tentatively classified 2,4-D as Interim Category C (possible human carcinogen), based on the Agency's "Guidelines for Carcinogen Risk Assessment", and subsequently presented its conclusions and all available information regarding 2,4-D's potential to cause cancer to the FIFRA Scientific Advisory Panel for consideration in June 1987.

III. SCIENTIFIC ADVISORY PANEL REVIEW

On June 25, 1987, the FIFRA Scientific Advisory Panel (SAP) met to review the data base supporting EPA's preliminary decision to classify 2,4-D as an Interim Class C carcinogen. The Panel was asked, "Does the Panel agree with the [Agency's Internal] Peer Review Committee's conclusion concerning the Interim Category C classification of the available 2,4-D oncogenicity data?."

On behalf of the Industry Task Force on 2,4-D Research Data, a number of expert witnesses provided written and oral comments to the Panel in an attempt to rebut the validity of the epidemiological and laboratory evidence. Comments concerning the epidemiological evidence were similar to those discussed in Units II.A. and IV of this notice. Regarding the laboratory evidence, one witness commented that the tumors noted in the rat study were not treatment-related because they failed to display certain commonly associated characteristics of this tumor type. The commentor also argued that the tumors in the high dose group were spontaneous in origin based on the presence of a brain tumor in one control animal.

In conclusion, the Panel issued the following written response on July 8, 1987:

> The SAP does not agree with the [Agency's Internal] Peer Review Committee's conclusion that the available 2,4-D oncogenicity data should be classified as

an Interim Category C (Possible Human Carcinogen). The Panel believes that the rat and mouse oncogenicity studies are adequate in design and conduct. The data are negative for oncogenicity in female rats and both sexes of mice. The increased incidence of astrocytomas in male rats exposed to 45 mg/kg 2,4-D was considered equivocal evidence of oncogenicity. The Panel believes that additional testing is required to resolve this issue. This testing should specifically address the astrocytoma issue by repeating an oncogenicity study. The study design should include two male rat control groups of 50 each and two male rat groups of the same size exposed to 45 mg/kg 2,4-D.

The Panel also believes that the human epidemiology studies represent well-designed and conducted investigations that present equivocal data on 2,4-D's oncogenicity for humans. Additional studies are underway that should help clarify the issue.

The Panel notes that equivocal evidence is different from limited evidence and that until additional data are developed it is improper to label 2,4-D as a

carcinogen or a noncarcinogen. The Panel therefore concludes that the present data for animals and humans are inadequate for determining oncogenicity and that 2,4-D should be classified in Group D (Not Classifiable as to Human Carcinogenicity).

Dated: July 8, 1987

Stephen L. Johnson

Executive Secretary,
FIFRA Scientific
Advisory Panel

The Agency's Peer Review Committee has deliberated on the scientific issues involving 2,4-D since the SAP meeting. The Agency now concurs with SAP's conclusions regarding the classification of 2,4-D with respect to carcinogenicity. The human and animal evidence of carcinogenicity is insufficient and, therefore, 2,4-D should be considered unclassifiable with respect to carcinogenicity (Category D). The Agency agrees with the SAP that the absence of strong statistical evidence in the rat does not support a finding of "limited" evidence of carcinogenicity. The Agency also agrees with SAP that additional testing is necessary in the rat in order to assess accurately 2,4-D's oncogenic potential in that species. This need is further supported by the concern that a MTD was

not reached in the rat and mouse studies. For that reason, the Agency will also require additional testing in the mouse.

IV. COMMENTS RECEIVED ON THE PRELIMINARY NOTIFICATIONS

Comments were received in response to the preliminary notifications on 2,4-D, 2,4-DB, and 2,4-DP from most registrants. The majority of these commentors concurred on a detailed comment received from the Industry Task Force on 2,4-D Research Data. In addition, several parties prepared comments on behalf of certain registrants regarding the benefits of 2,4-D as a growth regulator on citrus crops.

Although the comment received from the Task Force focused primarily on the NCI/Kansas epidemiology study, it also provided comments on existing animal data and other human epidemiology studies. The Task Force's basic position was that, "the Kansas study does not demonstrate an association between 2,4-D and non-Hodgkin's Lymphoma." Criticisms given by the Industry Task Force were for the most part similar to those raised by the Agency and independent reviewers. These included, but were not limited to, limitations in information collection regarding exposure to 2,4-D, limitations on the general accuracy of next-of-kin information, and the fact that the authors did not adequately examine confounding factors or discuss other possible causative agents (such as viruses).

Upon closer examination, the Agency and most reviewers agree that the NCI/Kansas study provides the basis for additional research, but that on its own, it does not provide a conclusive argument for associating farmer exposure to 2,4-D and non-Hodgkin's lymphoma. Some additional research is now underway at NCI. This research will hopefully help resolve this issue and determine whether such an association exists for 2,4-D.

Most commentors on the 2,4-DB and 2,4-DP preliminary notifications generally argued that these compounds should not be included in a review of 2,4-D. They pointed out basic differences in metabolism and the ostensible absence of 2,4-DB and 2,4-DP use in the Kansas study area.

The Agency generally agrees that 2,4-DB and 2,4-DP are sufficiently dissimilar toxicologically from 2,4-D to allow for a chemical-by-chemical type of evaluation. Therefore, the Agency will review these compounds individually and evaluate 2,4-D, 2,4-DB, and 2,4-DP in the reregistration process as separate compounds. Separate guidance documents for the reregistration of these pesticides are scheduled to be issued in 1988. However, within these pending evaluations, the Agency will continue to group the esters and salts of each active ingredient with the parent chemical.

The decision to issue separate guidance documents does not preclude the Agency from conducting a joint review of these compounds if at a later time data suggest metabolic or toxicologic similarities which would warrant such a simultaneous review.

V. AGENCY'S DECISION REGARDING SPECIAL REVIEW

Subsequent to the issuance of the preliminary notifications pursuant to 40 CFR 154.21, the findings of a NCI/Kansas epidemiologic study reporting an association between exposure to 2,4-D and human cancer was reviewed, at the Agency's request, by four National experts on epidemiology. These experts concluded independently that the study did not implicate 2,4-D alone as the causative factor for the Non-Hodgkin's lymphoma observed in this study, but rather indicated an association with phenoxy herbicide use in general. In addition, the FIFRA Scientific Advisory Panel reviewed this study, as well as the entire oncogenicity data base and concluded that 2,4-D should not be classified as a carcinogen or noncarcinogen at this time. Instead, the Panel recommended that 2,4-D be classified in Category D, Not Classifiable as to Human Carcinogenicity.

The Agency agrees with the external reviewers and SAP that the epidemiologic evidence as provided in the NCI/Kansas study does not raise as great a concern regarding 2,4-D as originally thought. The available human evidence, now considered inadequate by EPA on the basis of confounding factors and bias, does not establish a credible, causal relationship between 2,4-D and non-Hodgkin's lymphoma among Kansas farmers. Based on this conclusion, the Agency has determined that it will not conduct a Special Review of 2,4-D, or its structural analogs, 2,4-DB and 2,4-DP at this time.

The Agency now agrees with SAP that 2,4-D should be classified in Category D with respect to carcinogenicity (Not Classifiable as to carcinogenicity) based on the inadequate evidence of cancer in humans and laboratory animals.

Since the Agency is still interested in the results of further epidemiologic and laboratory studies on 2,4-D, the Agency may initiate a Special Review at a later time depending on the findings of such studies. In particular, NCI is currently evaluating human cancer cases and pesticide use in several other states in the U.S., which may have bearing on the continued registration of 2,4-D. In addition, the Agency will require additional testing in the rat and mouse. The Agency will also issue individual reregistration guidance documents on 2,4-D, 2,4-DB, and 2,4-DP in 1988, which will among other things involve intensive scrutiny of the entire available data bases and data deficiencies of these pesticides.

VI. PUBLIC COMMENT OPPORTUNITY AND PUBLIC DOCKET

The Agency is providing a 60-day period to comment on this Notice. Comments must be submitted by (insert date 60 days after date of publication in the FEDERAL REGISTER). All comments and information should be submitted in triplicate to the address given in this Notice under ADDRESS. The comments and information should bear the identifying notation OPP-30000/57. After receipt and evaluation of comments on this Notice, the Agency will publish a final decision in the FEDERAL REGISTER regarding whether or not a Special Review will be conducted.

The Agency has established a public docket (OPP-30000/57) for this proposal not to initiate a Special Review of 2,4-D, 2,4-DB, and 2,4-DP. This public docket will include this Notice; any other Notices pertinent to the Agency's decision regarding the Special Review of 2,4-D, 2,4-DB, and 2,4-DP; non-CBI documents and copies of written comments or other materials submitted to the Agency in response to the pre-Special Review registrant notifications and this Notice regarding Special Review of 2,4-D, 2,4-DB, and 2,4-DP; and a current index of materials in the public docket.

Dated: 14 Mar 88

John A. Moore,
Assistant Administrator,
Office of Pesticides and
Toxic Substances

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COPY OF THE ORIGINAL
Sandra Arts