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Part V

Environmental Protection Agency

Final Determination Concerning the Rebuttable Presumptions Against Registration for Certain Uses of Pesticide Products Containing 2,4,5-T and Silvex and Notice of Intent To Hold a Hearing

ENVIRONMENTAL PROTECTION AGENCY

[FRL-1373-7; OPP-30000/26E]

Final Determination Concerning the Rebuttable presumption Against Registration for Certain Uses of Pesticide Products Containing 2,4,5-T; Intent To Hold a Hearing To Determine Whether or Not Certain Uses of 2,4,5-T Should Be Canceled; Publication of Final Position Document Concerning All Non-Suspended Uses of 2,4,5-T

AGENCY: Environmental Protection Agency.

ACTION: Final notice of intent to hold a hearing concerning all non-suspended uses of pesticide products containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) to determine whether or not such uses should be canceled, and announcement of findings concerning the risks and benefits associated with such uses of 2,4,5-T products.

SUMMARY: On July 9, 1979, EPA announced its preliminary determination concerning the Rebuttable Presumption against Registration (RPAR) review of all uses of pesticide products containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) not suspended by prior Agency action, and proposed to hold a hearing to determine whether or not these uses of 2,4,5-T should be cancelled. See 44 FR 41531, July 17, 1979 (The "Preliminary Notice"). Pursuant to sections 6(b) and 25(d) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), copies of related decision documents were forwarded to the Secretary of Agriculture and the FIFRA Scientific Advisory Panel for comment.

This notice constitutes the final determination concerning the RPAR review for all non-suspended uses of 2,4,5-T. The Agency has determined that the potential oncogenic, fetotoxic, and teratogenic risks associated with these uses do not appear to be justified by offsetting economic, social, or environmental benefits and that such uses therefore appear to cause "unreasonable adverse effects on the environment," as defined by FIFRA Section 2(bb). The Agency has also determined that there are uncertainties in the data concerning the risks and benefits of the non-suspended uses, and that additional data relating to the determination of whether or not to cancel registrations for these uses can be developed for and through a hearing.

Accordingly, this notice (1) announces that the Agency will hold a hearing in accordance with FIFRA section 6(b)(2) to determine whether or not uses of 2,4,5-T products which have not been suspended should be canceled or reclassified, and (2) describes the procedure which should be followed by interested persons who wish to participate in the hearing to be held under section 6(b)(2).

FOR FURTHER INFORMATION CONTACT: Michael Dellarco, Project Manager, Special Pesticide Review Division (TS-791), Environmental Protection Agency, 401 M Street, S.W., Room 447, Washington, D.C. 20460, Telephone (202) 557-6244.

SUPPLEMENTARY INFORMATION: The Agency's final Position Document (PD 4) reviews specific findings concerning the risks and benefits of non-suspended uses of 2,4,5-T and contains a discussion of the comments of the FIFRA Scientific Advisory Panel and the Secretary of Agriculture on the Agency's preliminary findings and initial proposal to hold a hearing under section 6(b)(2). The PD 4 and the comments of the Scientific Advisory Panel and the Secretary of Agriculture are published in their entirety in the appendix to this notice.

I. Background

On April 11, 1978, the Environmental Protection Agency issued a notice of Rebuttable Presumption Against Registration (RPAR) for all pesticide products containing 2,4,5-T. See 43 FR 17110, April 21, 1978. Issuance of the RPAR initiated a comprehensive public review of all 2,4,5-T registrations and all pending applications for registration of 2,4,5-T products. On February 28, 1979, relying in large part on information developed and collected during the RPAR review, the Administrator ordered emergency suspension of, and issued notices of intent to cancel, the use of 2,4,5-T on forests, rights-of-way, and pastures (suspended uses), thereby terminating the RPAR review as to these uses of 2,4,5-T. See 44 FR 15874, March 15, 1979.

The RPAR review of the 2,4,5-T uses which were not subject to the suspension orders (non-suspended uses) continued. The non-suspended uses of 2,4,5-T include rice, rangeland, and non-crop uses.[1] Subsequently, on July 9, 1979, EPA announced its preliminary determination concerning the RPAR review of the remaining non-suspended uses of 2,4,5-T, and proposed to hold a hearing under FIFRA section 6(b)(2) to determine whether or not these uses of 2,4,5-T should be cancelled or reclassified. See 44 FR 41531, July 17, 1979. Copies of the Position Document (PD 2/3) summarizing the Agency's preliminary findings regarding the risks and benefits associated with the non-suspended uses and of the Agency proposal to hold a hearing were forwarded to the Secretary of Agriculture and the FIFRA Scientific Advisory Panel for comment, as required by sections 6(b) and 25(d) of FIFRA. Although not required to do so by FIFRA, the Agency also afforded registrants and other interested persons an opportunity to submit comments on the proposed action.

This notice constitutes the Agency's final determination concerning the RPAR review of the non-suspended uses of pesticide products containing 2,4,5-T and final decision concerning the proposal to hold a hearing under Section 6(b)(2) to determine whether or not the remaining uses of 2,4,5-T should be cancelled. In brief, the Agency has determined that the potential oncogenic, fetotoxic and teratogenic risks associated with these uses of 2,4,5-T do not appear to be justified by offsetting economic, social, or environmental benefits. Position Document 4, which is included in the appendix to this notice, summarizes the evidence on which this determination is based.

The Agency has also determined that further analysis of the risks and benefits of the non-suspended uses of 2,4,5-T will enable the Agency to decide whether or not registration of the remaining uses of 2,4,5-T should be cancelled or reclassified, and that pertinent information concerning the risks and benefits of these uses can be assembled and evaluated by holding a hearing pursuant to FIFRA section 6(b)(2). Pursuant to 40 CFR 164.32, the Agency intends to petition the Chief Administrative Law Judge to consolidate the hearing initiated by this notice with the cancellation hearing for suspended uses of 2,4,5-T and silvex. It is expected that a consolidated formal evidentiary hearing on cancellation of all 2,4,5-T registrations will begin early next year.

II. Legal Authority

A. General

In order to obtain a registration for a pesticide under FIFRA, a manufacturer must demonstrate that the pesticide satisfies the statutory standard for registration. That standard requires (among other things) that the pesticide

[1] The term "non-crop uses" refers to all other currently registered uses of 2,4,5-T, including use at the following sites: airports; fences; hedgerows (not otherwise included in suspended uses, e.g., rights-of-way, pasture); lumber yards; refineries; non-food crop areas; storage areas; wasteland (not otherwise included in suspended uses, e.g., forestry); vacant lots; tank farms; industrial sites and areas (not otherwise included in suspended uses, e.g., rights-of-way).

perform its intended function without causing "unreasonable adverse effects on the environment." FIFRA section 3(c)(5). "Unreasonable adverse effects on the environment" is defined 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." FIFRA section 2(bb).

In effect, this standard requires a finding that the benefits of each use of the pesticide exceed the risks of that use, when the pesticide is used in accordance with the terms and conditions of registration, or in accordance with widespread and commonly recognized practice. The burden of proving that a pesticide satisfies the registration standard is on the proponents of registration (e.g., registrants or users) and continues as long as the registration remains in effect. Under section 6 of FIFRA, the Administrator is required to cancel the registration of a pesticide or modify the terms and condition of registration whenever he determines that the pesticide no longer satisfies the statutory standard for registration.

B. The RPAR Process

The Agency created the rebuttable presumption against registration (RPAR) process to facilitate the identification of pesticide uses which may not satisfy the statutory standard for registration and to provide a structure for the gathering and evaluation of information about the risks and benefits of these uses. The structure permits public participation at major points in the evaluation process.

The regulations governing the RPAR process are set forth at 40 CFR 162.11. This section provides that a rebuttable presumption shall arise if a pesticide meets or exceeds any of the risk criteria identified in the regulations. After an RPAR is issued, registrants and other interested persons are invited to review the data upon which the presumption is based and to submit data and information to rebut the presumption. Respondents may rebut the presumption of risk by showing that the Agency's initial determination of risk was in error, or by showing that exposure of man or other sensitive species which is likely to be associated with use of the pesticide will not result in a significant risk of adverse effects of the type in question. Further, in addition to submitting evidence to rebut the risk presumption, respondents may submit evidence as to whether the economic, social and environmental benefits of the use of the pesticide subject to the presumption outweigh the risk of use.

The regulations require the Agency to conclude an RPAR by issuing a Notice of Determination in which the Agency states and explains its position on the question of whether the RPAR risk presumptions have been rebutted. If the Agency determines that the presumption has not been rebutted, it then considers information relating to the social, economic, and environmental costs and benefits of use of the pesticide, including information which registrants, the U.S. Department of Agriculture, and other interested persons have submitted to the Agency, and other benefits information known to the Agency. If the Agency determines that the risks of a particular pesticide use appear to outweigh its benefits, the Agency may elect to conclude the RPAR process by issuing a notice of intent to cancel, deny, or reclassify registration of the pesticide for the use in question, pursuant to FIFRA sections 6(b)(1) and 3(c)(6), or by issuing a notice of intent to hold a hearing to determine whether or not registration for that use should be cancelled, denied, or reclassified, pursuant to FIFRA section 6(b)(2).

C. Choice of Mode of Action

Two types of proceedings are available under section 6(b) of FIFRA to cancel a pesticide registration, or to modify the terms and conditions of its registration: FIFRA section 6(b)(1) proceedings and FIFRA section 6(b)(2) proceedings. In general, FIFRA section 6(b)(1) proceedings begin with a notice specifying the regulatory action which the Administrator is proposing. This action takes effect automatically, without hearings, at the expiration of a notice period prescribed by statute, unless a registrant or a person adversely affected by the notice requests a hearing within that period. If a hearing is requested, the regulatory action proposed by the Administrator does not take effect; however, at the conclusion of the hearing, the Administrator may implement the proposed action, if he determines that it is appropriate to do so based on the record developed in the hearing.

Section 6(b)(2) proceedings, on the other hand, begin with a general notice specifying the issues which the Administrator desires to have explored at a hearing. Unlike section 6(b)(1) proceedings, the section 6(b)(2) proceeding does not include an initial proposed regulatory solution which would take effect automatically if a hearing is not requested. Interested persons may participate in the hearing; at the conclusion of the hearing, the Administrator may take whatever action he deems appropriate, based upon the record developed in the hearing, including cancellation of a pesticide registration or modification of the terms and conditions of its registration.

The judgment of whether to issue a FIFRA section 6(b)(1) or a section 6(b)(2) notice is within the sole discretion of the Administrator (or his duly designated delegatee). If the Administrator determines that the risks of a pesticide use appear to outweigh its benefits, he may issue a notice of intent to cancel pursuant to FIFRA section 6(b)(1). If, however, the Administrator's judgment concerning the risks and benefits associated with a particular pesticide use or the appropriate regulatory response is only tentative, the Administrator may issue a notice under FIFRA section 6(b)(2) declaring his intention to hold a hearing "to determine whether or not its registration should be cancelled."

D. External Review

The statute requires the Agency to submit notices to be issued pursuant to FIFRA section 6 to the Secretary of Agriculture, along with an analysis of the impact of the proposed action on the agricultural economy. FIFRA section 6(b). The Agency must submit these documents to the Secretary of Agriculture at least 60 days before issuing the the notice in final form. If the Secretary of Agriculture comments, in writing, within 30 days after receiving the notice, the Agency is required to publish the Secretary's comments and the Administrator's responses to them along with the notice. FIFRA also requires the Administrator of submit FIFRA section 6 notices, at the same time and under the same procedures as those described above for review by the Secretary of Agriculture, to the Scientific Advisory Panel for comment on the impact of the proposed action on health and the environment. FIFRA section 25(d).

Although not required to do so under FIFRA, the Agency has determined that it is consistent with the general theme of the RPAR process and the Agency's overall policy of open decisionmaking to afford registrants and other interested persons an opportunity to comment on the bases for the proposed action during the time that the proposed action is under review by the Secretary of Agriculture and the Scentific Advisory Panel. Accordingly, appropriate steps were taken to make copies of Position Document 2/3 on the non-suspended uses of 2,4,5-T available to registrants and other interested persons at the time the preliminary decision documents were transmitted for formal external review, through publication of a notice

of availability in the Federal Register, and by other means. Registrants and other interested persons were allowed the same period of time to comment—30 days—that FIFRA provides for receipt of comments from the Secretary of Agriculture and the Scientific Advisory Panel.

The decision to issue a FIFRA section 6 notice is a preliminary determination, pending external review and Agency analysis of comments received. On the basis of these comments, the Agency may withdraw the notice, issue a final notice without modification, or modify the notice, as appropriate.

III. Determinations and Announcement of Regulatory Actions

As detailed in the Preliminary Notice and PD 2/3, the Agency considered information on the risks associated with the non-suspended uses of 2,4,5-T, including information submitted by registrants and other interested persons in rebuttal to the 2,4,5-T RPAR. The Agency also considered information on social, economic and environmental benefits of the non-suspended uses of 2,4,5-T, including benefits information submitted by registrants and other interested persons in conjunction with their rebuttal submissions and information submitted by the United States Department of Agriculture. The Agency's assessment of the risks and benefits of the non-suspended uses of 2,4,5-T, its conclusions and determinations that the non-suspended uses of 2,4,5-T appear to cause unreasonable adverse effects on the environment, and its determination that a section 6(b)(2) hearing on these uses is warranted, were set forth in detail in PD 2/3. The PD 2/3 was adopted by the Agency as its statement of reasons for the determinations and actions announced in the Preliminary Notice.

This notice constitutes the Agency's final notice of determination concluding the RPAR on the non-suspended uses of 2,4,5-T. It reflects any modifications in the Agency's initial determinations on the risks and benefits of non-suspended 2,4,5-T pesticide uses which the Agency has concluded are appropriate, after review of the comments and information received concerning PD 2/3 and the Preliminary Notice from the Secretary of Agriculture, the SAP, and other sources. This notice also indicates that there is no modification of the regulatory action announced in the Preliminary Notice.

PD 4, which accompanies this notice, discusses in detail the comments that were received from the SAP and the Secretary of Agriculture,[2] the Agency's response to these comments and the Agency's reasons for changing or not changing its initial determinations and the regulatory action announced in the Preliminary Notice. Finally, this notice announces the regulatory action which the Agency is implementing concerning 2,4,5-T. The Agency hereby incorporates PD 2/3 and PD 4 as its statement of reasons for this action.

A. Determinations on Risks

The 2,4,5-T RPAR was based on information indicating that 2,4,5-T and/or its TCDD contaminant pose oncogenic, fetotoxic and teratogenic risks to the human population. The Agency has determined that information submitted to rebut these risk criteria was insufficient to remove the Agency's concerns that 2,4,5-T and/or TCDD pose risks of fetotoxic and teratogenic effects in unborn children, and that 2,4,5-T and/or TCDD pose risks of increased incidences of cancer among exposed populations. The Agency has determined that the rangeland, rice and non-crop area uses of 2,4,5-T create opportunities for human exposure to this chemical and TCDD and that such exposure appears generally to cause adverse human effects.[3] The Agency has therefore concluded that the oncogenic, fetotoxic and teratogenic risks associated with the non-suspended uses of 2,4,5-T are of sufficient magnitude to require the Agency to determine whether these uses of 2,4,5-T offer social, economic or environmental benefits which offset these risks.

B. Determination of Benefits

The uses of 2,4,5-T which are subject to this notice fall into three categories: rangeland, rice and non-crop uses. For each of these use categories an estimate of the economic impact of cancellation has been made. These estimates are intended only as approximations based on available information.[4] The Agency's analysis of this information leads it to conclude that the benefits of 2,4,5-T for the three categories of uses are roughly as set forth below.[5]

(1) *Rangeland.*[6] There are an estimated one billion acres of rangeland and pasture suitable for grazing in the contiguous 48 states, plus 351 million acres in Alaska and 3 million acres in Hawaii. About 90 percent of this total acreage is rangeland. Of this total, about one percent is treated with herbicides, primarily 2,4,D.

2,4,5-T is used to control various wood and herbaceous plants on about 1,500 acres of rangeland. The most important weed species treated are mesquite and several species of oak. Cactus, yucca, poisonous plants, and desert shrubs are also treated with 2,4,5-T to a lesser extent.

The estimated impact on farm income and beef prices of cancelling 2,4,5-T on range would be slight. When compared with the U.S. total farm value of beef production (about $15 billion annually), these impacts, averaging less than $16.5 million annually, are relatively small (0.1 percent). In those local areas where target weed species are a problem, local farm income may be affected significantly. Adequate information to evaluate such local impacts is not available. At the retail level, cancellation of 2,4,5-T for use on rangeland could cause the consumer price index for food and beverages to increase by a maximum of 0.05 percent, an insignificant increment.

(2) *Rice.* Over 99 percent of the 2.5 million acreas of U.S. rice-growing acres are located in Arkansas, Louisiana, Texas, Mississippi and California. 2,4,5-T is currently used to control broadleaf and aquatic weeds on an estimated 300,000 acres in the lower Mississippi Valley area comprising about 12 percent of U.S. rice acres.

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[2] The comments from the SAP and the Secretary of Agriculture are attached as appendices to PD 4. All other comments are available in the 2,4,5-T public file for inspection and review.

[3] The Agency is continuing to collect and review new laboratory data on the toxic effects of these chemicals in animals, and monitoring data on residues of these chemicals in environmental media.

[4] The Agency is continuing to collect and review data relating to the benefits of 2,4,5-T for range, rice, and non-crop uses.

[5] For purposes of this analysis it is assumed that silvex would also be cancelled and, therefore, would not be available as an alternative to 2,4,5-T. In view of the virtually identical toxicological characteristics of the two compounds and the similarity of the benefits of both, it is unlikely that one would be cancelled and not the other.

[6] In response to comments expressing confusion about the Agency's range and pasture definitions, provided in PD 2/3 and in the 2,4,5-T Suspension order the March 15, 1979 (44 FR 15874), respectively, the Agency is modifying its range definition and correcting an inadvertent error in its pasture definition:

"Range" is now defined as non-pasture grazing land producing forage from native plant species or introduced species managed as native species. Grazing land which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application or other similar practices applied to it is excluded. Forests, defined as lands capable of growing 20 cubic feet of wood per year of desirable species which are not withdrawn for non-timber purposes, are also excluded.

"Pasture" is now defined as land producing forage for animal consumption, harvested by grazing, which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application or other similar practices applied to it. Fencerows enclosing pasture are included as part of the pasture.

The modifications in the definitions do not require any modification of the benefits analysis because that analysis was premised on these definitions.

Propanil and 2,4-D are the most likely substitutes for 2,4,5-T for control of rice weeds. These chemicals are thought to be generally less effective than 2,4,5-T for control of the major rice weeds; thus yield and quality reductions may occur where propanil and 2,4-D are used to replace 2,4,5-T. The substitution of these chemicals for 2,4,5-T could result in production reductions of less than 0.1% of national production.

If 2,4,5-T is cancelled for use on rice, annual producer weed control cost increases and production losses are estimated at about $6 million per year. Prices received by farmers, and ultimately paid by consumers, could increase by about five percent within three years. Since rice comprises only a small portion of the U.S. consumer's diet (comsuption of milled rice is less than eight pounds per capita annually), price increases of this magnitude will have only minor impacts on consumers.

(3) *Non-crop uses.*[7] 2,4,5-T is registered for control of many broadleaf and herbaceous weeds in a variety of urban and rural non-crop areas such as hedgerows, storage areas, and vacant lots. It is believed that only 11% (190,000 acres) of all non-crop areas treated with herbicides are treated with 2,4,5-T annually.

Both chemical and non-chemical controls are available as alternatives to 2,4,5-T for chemical control in non-crop areas. The chemical alternatives include 2,4-D, picloram, dicamba, AMS, and amitrole. Non-chemical controls include mechanical methods, such as mowing or shearing, and manual methods. The relative efficacy of the alternatives in comparison to 2,4,5-T is unknown. However, it is believed that chemical alternatives, either in multiple applications or in combination, will be widely substituted for 2,4,5-T and will provide equivalent control.

C. Determination on Apparent Unreasonable Adverse Effects

For the reasons set forth in detail in PD 2/3, and as further discussed in PD 4, the Agency has made the following determinations relating to the apparent unreasonable adverse effects of the non-suspended uses of 2,4,5-T:

(1) *Determinations on Rangeland Use.* The Agency has determined that the use of 2,4,5-T on rangeland appears to pose risks which are greater than the social, economic, and environmental benefits of the use. The Agency has further determined that the data submitted and reviewed during the RPAR review on the exposure potential and benefits of the rangeland use are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of 2,4,5-T on rangeland appears generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(2) *Determinations on Rice Use.* The Agency has determined that the use of 2,4,5-T on rice appears to pose risks which are greater than the social, economic and environmental benefits of the use. The Agency has further determined that data submitted and reviewed during the RPAR review on the exposure potential and benefits of the rice use are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of 2,4,5-T on rice appears generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(3) *Determinations on Non-Crop Uses.* The Agency has determined that the use of 2,4,5-T on airports, fences, lumber yards, refineries, non-food crop areas, storage areas, wastelands, vacant lots, tank farms, industrial sites and other uses not subject to the emergency suspension orders (i.e., forests, rights-of-way, and pastures) appear to pose risks which are greater than the social, economic and environmental benefits of those uses. The Agency has further determined that data submitted and reviewed during the RPRA review of the exposure potential and benefits of the non-crop uses are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the agency has determined that the non-crop uses of 2,4,5-T appear generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

D. Announcement of Regulatory Actions

Based upon the determinations summarized above, and developed in detail in PD 2/3 and PD 4, the Agency is announcing the following regulatory actions, and this document shall constitute its initiation of these actions:

(1) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the rangeland use of 2,4,5-T;

(2) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the rice use of 2,4,5-T; and

(3) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the non-crop uses of 2,4,5-T.

IV. Statement of Issues

In accordance with § 164.23 of the Agency's Rules of Practice (40 CFR Part 164), this part of the notice states the questions on which evidence relative to the non-suspended uses of 2,4,5-T shall be taken at the FIFRA section 6(b)(2) hearing.

With respect to the rice, rangeland, and non-crop uses of 2,4,5-T, evidence will be taken as to the following questions:

(1) Whether the use of 2,4,5-T on rangeland generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(2) Whether the use of 2,4,5-T on rice generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(3) Whether the non-crop uses of 2,4,5-T generally cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(4) Whether the use of 2,4,5-T on rice, rangeland, or non-crop areas will generally cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice unless the terms and conditions of registration are modified to be more restrictive than those currently in effect;

(5) Whether, if modifications to the terms and conditions of registration are adopted, the labeling of 2,4,5-T products for these uses will comply with the applicable provisions of FIFRA; and

(6) Whether, despite modification of the terms and conditions of registration, the use of 2,4,5-T on rice, rangeland, or non-crop areas will generally cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice and should thus be cancelled.

[7] "Non-crop uses" include: airports; fences; hedgerows (not otherwise included among the previously suspended uses, e.g., rights-of-way, pasture); lumber yards; refineries; non-food crop areas; storage areas; wastelands (not otherwise included among the previously suspended uses, e.g., forestry); vacant lots; tank farms; industrial sites and areas (not otherwise included among the previously suspended uses, e.g. rights-of-way).

V. Procedural Matters

A. Procedure for Participating in the 6(b)(2) Hearing

Hearings concerning notices issued under section 6(b)(2) of FIFRA are initiated solely at the discretion of the Agency and concern all registrations and uses identified in the statement of issues in the notice.[8] Interested persons may participate in hearings convened by the Agency under FIFRA Section 6(b)(2) by filing a timely response in accordance with 40 CFR 164.24.

Section 6(b) of FIFRA provides that any "decision pertaining to registration or classification" of a pesticide which is issued after completion of a Section 6(b)(2) hearing "shall be final." Thus, all registrants and other adversely affected parties who might be affected by cancellation or reclassification of the non-suspended uses of 2,4,5-T should be aware that participation in the hearing initiated by this notice may constitute their *sole* opportunity to present evidence and/or testimony concerning relating issues prior to *final* Agency action. Moreover, judicial review under FIFRA section 16(b) of any action concerning the non-suspended uses of 2,4,5-T which is taken by the Administrator at the conclusion of the Section 6(b)(2) hearing can only be obtained by a person who has been "a party to the proceedings . . ."[9]

All persons who request participation in the hearing initiated by this notice must follow the Agency's Rules of Practice Governing Hearings, 40 CFR Part 164. Section 164.24 of the Rules of Practice provides that each person who wishes to participate in the hearing initiated by this notice must file a written response which satisfies the following requirements: (1) the response must state the person's position and interest concerning the issues identified in Section IV of this notice; (2) if the person is a registrant or an applicant for registration, the response must specifically identify the registration or application number of each affected pesticide product and include a copy of the currently accepted and/or proposed labeling and a list of the currently registered or proposed uses for each affected pesticide product; and (3) the response must be *received* by the Hearing Clerk within thirty (30) days of publication of this notice in the **Federal Register**. Failure to comply with these requirements will automatically result in denial of the request to participate in the hearing initiated by this notice.

Requests for hearings must be submitted to: Hearing Clerk (A-110), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, D.C. 20460.

b. Ex Parte Communications

The Agency's Rules of Practice for hearings conducted pursuant to section 6 of FIFRA forbid the Administrator, the Judicial Officer, and the Administrative Law Judge, at all stages of the proceedings, from discussing the merits of the proceedings *ex parte* with any party or with any person who has been connected with the preparation or presentation of the proceeding as an advocate or in an investigative or expert capacity, or with any of their representatives. 40 CFR 164.7.

Accordingly, the following Agency offices, and the staffs thereof, are designated to perform all investigative and prosecutorial functions in this case: the Office of the Deputy Administrator, the Office of Toxic Substances, the Office of Pesticide Programs, the Office of General Counsel, and the Office of Enforcement.

From the date of this notice until any final decision, neither the Administrative Law Judge, the Judicial Officer, nor the Administrator shall have any *ex parte* contact or communication with any investigative or trial staff employee, or any other interested person not employed by EPA, on any of the issues involved in this proceeding. However, persons interested in this proceeding should feel free to contact any other EPA employee, including both investigative and trial staff, with any questions they may have.

Dated: December 3, 1979.

Steven D. Jellinek,

Assistant Administrator for Pesticides and Toxic Substances.

[8] In contrast, hearings concerning notices of regulatory action issued under Section 6(b)(1) of FIFRA are held only if a registrant or other adversely affected party files a valid and timely hearing request and concern only those registrations and uses which are identified in such hearing requests.

[9] It is anticipated that the Section 6(b)(2) hearing initiated by this notice will be consolidated with the Section 6(b)(1) cancellation hearing concerning the suspended uses of 2,4,5-T and silvex. Thus, it is possible that any person who is already a party in the 6(b)(1) proceeding may be able to obtain judicial review of final Agency action concerning the non-suspended uses of 2,4,5-T without filing a separate request to participate in the 6(b)(2) proceeding. However, since consolidation of the proceedings is a matter within the sole discretion of the Chief Administrative Law Judge, the Agency recommends that any party who might desire to seek review of any final Agency action concerning currently permissible uses of 2,4,5-T should file a timely response under 40 CFR § 164.24.

2,4,5-T/Silvex Position Document 4—U.S. Environmental Protection Agency, Section Head: Kyle Barbehenn

Position Document 4 for Certain Uses of 2,4,5,-Trichlorophenoxyacetic Acid (2,4,5-T) and 2-(2,4,5-Trichlorophenoxy) Propionic Acid (Silvex)

This document represents the conclusion of the Rebuttable Presumption Against Registration (RPAR) process for 2,4,5-T and silvex, and contains the Agency's final determination on regulatory action regarding the use of 2,4,5-T and silvex which were not suspended on February 28, 1979. In summary, the Agency has reviewed the comments received on its decision, principally those of the FIFRA Scientific Advisory Panel (SAP) and the United States Department of Agriculture (USDA), and now reaffirms its preliminary decision to hold FIFRA 6(b)(2) hearings to determine whether or not to cancel these uses of 2,4,5-T and silvex.

I. Background

On April 11, 1978, the Environmental Protection Agency ("the Agency") issued a notice of rebuttable presumption against registration and continued registration of all pesticide products containing the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) [43 FR 17116, April 21, 1978]. Issuance of the RPAR began the Agency's public review of the registered uses of 2,4,5-T and the uses for which applications for registration are pending. Later, on February 28, 1979, the Administrator ordered the emergency suspension of the use of 2,4,5-T on forests, rights-of-way, and pastures (suspended uses) [44 FR 15874, March 15, 1979].[1] The RPAR review continued for the use of 2,4,5-T on rice, range,[2] and certain non-crop sites (non-suspended uses).

When the suspension orders were issued, silvex was a candidate for RPAR review, but an RPAR notice had not been issued. However, the use of silvex on forests, rights-of-way, pastures, homes and gardens, aquatic areas/ditch banks, and commercial/ornamental turf was included in the suspension orders

[1] Data and analyses developed in connection with the RPAR review led the Administrator to issue the emergency suspension orders and related notices of intent to cancel the suspended uses of 2,4,5-T and silvex. Suspension hearings began on April 19, 1979, but were discontinued on May 15, 1979, after all registrants withdrew from the hearings and petitioned the Administrator for an expedited cancellation hearing. The formal evidentiary phase of the cancellation hearing is scheduled to begin on January 22, 1980.

[2] See Appendix A, for a clarification of the definition of pasture (suspended use) and rangeland (non-suspended use).

[44 FR 15897, March 15, 1979] because both 2,4,5-T and silvex contain the highly toxic contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), both have comparable uses and correspondingly comparable exposure potential, and both pose risks of adverse effects which are similar in many ways.

The RPAR review of 2,4,5-T and the suspension action prompted the Agency to expedite its RPAR review of the uses of silvex which had not been suspended, namely the use on rangeland, rice, sugarcane, orchards, and non-crop areas[3] (non-suspended uses). As a result of this expedited review, the Agency determined that the non-suspended uses of silvex exceed both the oncogenic and other chronic or delayed toxic effects risk criteria for issuance of an RPAR [40 CFR 162.11(a)(3)].

On July 9, 1979, the Agency issued preliminary notices of determination relating to the non-suspended uses of 2,4,5-T and silvex (44 FR 41531; 44 FR 41536, July 17, 1979). The Agency considered risk information concerning the non-suspended uses of 2,4,5-T and silvex and found (1) that 2,4,5-T and silvex are fetotoxic and teratogenic and (2) that 2,3,7,8 tetrachlorodibenzo-*p*-dioxin (TCDD), the trace contaminant in 2,4,5-T and silvex, is fetotoxic, teratogenic and carcinogenic. The Agency acknowledged that there are some uncertainties about the amount of human exposure to 2,4,5-T, silvex, and TCDD because of the limited exposure information available.

[3] See Table 1.

Table 1.—*Suspended and Nonsuspended Uses of 2,4,5-T and Silvex*

	2,4,5-T	Silvex
Nonsuspended uses. (2,4,5-T RPAR issued April 21, 1978 (43 FR 17116); silvex RPAR issued July 17, 1979 (44 FR 41536))	Rice, range, noncrop sites [1].	Rice, range, noncrop sites,[1] sugarcane, orchards.
Suspended uses. (2,4,5-T emergency suspension issued March 15, 1979 (44 FR 15874); silvex emergency suspension issued March 15, 1979 (44 FR 15897)).	Forests, rights-of-way pasture.	Forests, rights-of-way, pasture, home and garden, aquatic areas/ditch banks, commercial/ornamental turf.

[1] Includes use on or around noncrop sites, such as fencerows, hedgerows, fences (not otherwise included in suspended uses, e.g., rights-of-way, pasture), industrial sites or buildings (not otherwise included in suspended uses, e.g., rights-of-way, commercial/ornamental turf), storage areas, waste areas, vacant lots, parking areas, and all other noncrop sites.

Concerning the non-suspended uses of 2,4,5-T and silvex, the Agency has also considered economic benefits information which pesticide registrants, the United States Department of Agriculture, and other interested parties originally submitted in response to the 2,4,5-T RPAR notice. During the course of the review, the Agency weighed risks and benefits to determine whether or not the risks of each use were exceeded by the corresponding benefits. The Agency determined that additional benefits data were being developed which merit consideration, especially for the non-suspended uses of silvex.

Accordingly, with respect to the non-suspended uses of 2,4,5-T and silvex, the Agency has concluded: (1) that continued use of these two chemicals appears to cause unreasonable adverse effects on the environment, (2) that there are uncertainties in the data relating to the risks and benefits of the uses at issue, (3) that additional data on the risks and benefits of the non-suspended uses of 2,4,5-T and silvex will permit the Agency to determine whether or not to cancel the registrations for these uses, and (4) that such information can be acquired through a public hearing under section 6(b)(2) of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, 7 U.S.C. 136 *et seq.* (FIFRA).

Under FIFRA, the Agency is required to submit these preliminary determinations to the Scientific Advisory Panel for comment on risk issues, and to the United States Department of Agriculture for comment on benefits issues. The Agency must then respond publicly to the comments made by the SAP and the USDA before making a final regulatory decision (7 U.S.C. 136d). The remainder of this document sets forth the Agency's analysis of comments submitted by USDA, the SAP, and other interested parties, and the Agency's reasons and the factual base for the action it is taking. The formal comments submitted by the SAP and the USDA are reproduced in their entirety as Appendices B and C of this document.

II. Issues Relating to Risk

A. Comments Relating to Toxicity

The Agency's proposed action is based in part on data that show 2,4,5-T, silvex, and/or TCDD produce fetotoxic, teratogenic, and carcinogenic effects in test animals. The SAP agreed with the Agency's assessment of the toxic effects of these chemicals but did not fully agree on all aspects of its interpretation of dose level responses.

(1) *Reproductive Toxicity.* In previous position and suspension documents, the Agency cited numerous studies in test species which showed that 2,4,5-T or silvex containing 0.5 parts per million (ppm) or less TCDD and pesticide-free TCDD produce cleft palate, kidney abnormalities, delayed ossification, fetal mortality, and reduced fetal weight (see 43 FR 17116, April 21, 1978 and 44 FR 15874, March 15, 1979 for review). In rodents, adverse effects were noted at maternal doses as low as 10 milligrams per kilogram (mg/kg) body weight 2,4,5-T (0.05 ppb TCDD) [Smith, 1978]; 50 mg/kg silvex body weight (<0.05 ppm TCDD) [Dow, 1973]; and 0.001 micrograms per kilogram (ug/kg) body weight TCDD (Murray, 1979; Smith et al., 1976). Furthermore, in non-human primates, maternal doses of TCDD as low as 50 parts per trillion (ppt) (about 0.002 ug/kg) resulted in reduced fertility and increased fetal loss (Schantz et al., 1979). Similar and more severe effects have been observed at higher doses in all species tested. Because statistically significant effects consistent with those seen at higher doses were observed at 0.001 ug/kg TCDD in a three generation study in rats, and because this is the lowest dose tested in any species, the Agency has determined that a non-observed effect level (NOEL) has not been demonstrated for fetotoxic effects due to TCDD exposure.

The SAP agreed with the Agency that 2,4,5-T, silvex, and TCDD are each teratogenic and fetotoxic. The SAP also agreed that a NOEL had not been established for TCDD in monkeys. However, the SAP concluded that "for all practical purposes" a NOEL has been shown for TCDD in studies with rats and mice. Although the SAP concluded that 0.001 ug/kg was a practical NOEL, the Panel also recognized the existence of effects at this dose level. While the Agency interpreted these effects as significant, and sufficient to preclude establishment of a NOEL, the Panel interpreted them as suggestive of a NOEL.

Without additional data, the Agency is reluctant to adopt the Panel's interpretation. TCDD is one of the most toxic chemicals known. Its degree of

toxicity, as well as its toxic manifestations, varies among the animal species, and its effects on the human reproductive system are largely unknown. In addition, the control data upon which the study is based are so variable as to warrant concern that these fluctuations may be masking additional effects. Because the effects seen at 0.001 ug/kg are consistent with those seen at higher doses, and because of the factors listed above, the Agency is unwilling to dismiss the effects observed at 0.001 ug/kg as insignificant to risk assessment. Extrapolations from experimental animal studies to man are difficult even when there is a clear NOEL. When, with TCDD, there is no NOEL, the Agency would prefer to err on the side of safety.

(2) *Oncogenicity.* In Position Document 2/3 on 2,4,5-T and Position Document 1/2/3 on silvex, the Agency concluded that commercial 2,4,5-T and silvex may pose a significant carcinogenic risk to exposed humans. This conclusion was based primarily on data showing that TCDD, an unavoidable contaminant in commercial 2,4,5-T and silvex, is carcinogenic in laboratory animals.

The principal comments made by the SAP regarding the oncogenicity of 2,4,5-T, silvex, and TCDD, together with the Agency's response to these comments, are summarized below.

The SAP agreed with the Agency that TCDD is carcinogenic in laboratory animals. The SAP also agreed that commercial 2,4,5-T products pose some oncogenic risk to man because of contamination of these products with TCDD. However, the SAP concluded that the available evidence indicates that there is no substantial oncogenic risk to man from exposure to commercial 2,4,5-T.

The Agency disagrees with this conclusion. When the SAP considered the Agency's proposed section 6(b)(2) notices for 2,4,5-T and silvex, the Agency had not yet completed its exposure analysis. The exposure information provided to the SAP was thus not a sufficient basis for making an accurate determination on whether or not the oncogenic risk posed by the uses of 2,4,5-T affected by the proposed notices was substantial. An accurate determination may be possible when the Agency completes its exposure analysis.

The SAP stated that the CAG concluded that the non-oncogenic dose [in the study by Kociba et al. (1978) on TCDD] lies between 0.01 and 0.001 mg/kg/day. The Agency, however, contends that the CAG concluded only that no oncogenic response was *observed* in the Kociba study at a dose of 0.001 mg/kg/day. On the basis of the no-threshold dose response theory regarding carcinogenicity (Albert et al., 1977), the CAG and the Agency consider any dose of TCDD, no matter how small, to pose some carcinogenic risk to humans.

The SAP concluded that the few oncogenicity studies on silvex which have been conducted do not indicate any oncogenic effects, but commented nonetheless that "these data must be viewed with some caution because of the contamination of commercial silvex with TCDD."

The Agency agrees with the SAP that any chronic studies on silvex which have not demonstrated a carcinogenic response should be viewed with caution. Because TCDD is an unavoidable contaminant of commercial silvex, the Agency concludes that silvex poses some carcinogenic risk to exposed humans. A determination of the substantiability of this risk may be possible when the Agency completes its exposure analysis.

Certain other comments by the SAP reflect differences of opinion among scientists concerning other technical details which have no direct bearing on the Agency's proposal to hold a 6(b)(2) hearing. Such a hearing provides an appropriate forum for an in-depth development and analysis of the issues and the Agency thus feels that it is not necessary to respond to several of the SAP's comments on oncogenicity at this time.

B. Comments Relating to Exposure and Risks

On the question of potential human exposure to 2,4,5-T, silvex, and/or TCDD from the non-suspended uses, the Agency and the SAP are in agreement on the need for additional data. In reaching a preliminary decision, the Agency concluded that although the non-suspended uses appear to cause unreasonable risks of adverse effects, at present, gaps in the data preclude an accurate assessment of the potential for human hazards. In particular, the Agency specified a need for additional information on possible avenues of human exposure. The SAP also concluded that there is a potential for human exposure from the non-suspended uses, but that the available data are "incomplete and preliminary in nature". The SAP specifically recommended that additional monitoring data be obtained from sources likely to demonstrate human exposure, placing particular emphasis on TCDD levels.

(1) *Monitoring Data.* In the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, the Agency presented data from STORET, a computerized data base of surface water chemical residues, and from the National Surface Water Monitoring Program for Pesticides (NSWMPP), which indicate that 2,4,5-T and silvex residues were present in water in areas where these herbicides are used. The Agency acknowledged that these residues could not be attributed to specific uses of 2,4,5-T and silvex. However, the Agency's concern about these residues in the environment was supported by monitoring studies in rangeland (Marigold and Schulze, 1969; Lawson, 1976) and apple orchard areas (Cochran et al., 1976).

Concern about potential human exposure to 2,4,5-T, silvex, and/or TCDD from the non-suspended uses has prompted the Agency to undertake new monitoring studies. As indicated in the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, rice, crayfish, catfish, water, and sediment from the South are being tested to determine the extent of environmental contamination due to 2,4,5-T and silvex use on rice. The Agency is also engaged in monitoring edible fish, rice, sediment, human milk, beef fat, and beef liver for TCDD residues.

During the SAP meeting of August 15, 1979, the Agency acknowledged that there is not a large body of monitoring data available for specific uses because previously reported monitoring projects were rarely use-oriented and were frequently conducted at times when the chemical was not being used in the monitored area. Therefore, residues traceable to a particular chemical use might not be detected under these circumstances.

The SAP concurred with the Agency's view that available monitoring data are inadequate to assess potential human exposure from the uses of 2,4,5-T on rice, range, and certain non-crop sites, and from the use of silvex on orchards, rice, range, sugarcane, and certain non-crop sites. The SAP characterized the monitoring data presented by the Agency as incomplete and preliminary in nature and recommended that additional data be gathered regarding the levels of 2,4,5-T, silvex, and TCDD in milk, tissues of range animals and edible aquatic organisms.

As indicated above, the Agency is currently conducting several significant monitoring studies in the media recommended by the SAP. In addition, the Agency is reviewing recent monitoring studies by other researchers, such as another TCDD study in human milk (Memo, 1979c) and a TCDD study in fish (Kuehl et al., 1979). The results of

these studies will be reviewed during the 6(b)(2) hearings.

(2) *Risk Comments.* The SAP made several comments on the issues of exposure and risk, and on the methods of risk reduction with which the Agency disagrees. The Panel concluded that the margins of safety between exposure and the NOEL were sufficient to protect the general population from any reproductive risk associated with the non-suspended uses of 2,4,5-T and silvex. Concerning mixers and loaders, the SAP suggested that risk could be reduced to a safe level by the use of protective clothing and equipment. The Agency's disagreement with the Panel's adoption of a "for all practical purposes" NOEL for TCDD has been discussed above. The Agency further questions whether the existing data are sufficient to permit the Panel's conclusion that protective clothing and equipment are sufficient to adequately reduce risk for mixers and loaders.

In addition, the SAP recommended that efforts be made to reduce the TCDD content in commercial 2,4,5-T and silvex. Although the Agency applauds any efforts by registrants to reduce TCDD levels in pesticide products containing 2,4,5-T and silvex, any review of these chemicals at this time can be based only on the present formulations of 2,4,5-T and silvex products which unavoidably contain TCDD. As for all other pesticides, 2,4,5-T and silvex registrants must provide the Agency with scientific data, through the registration process, that the production of 2,4,5-T and/or silvex without TCDD does not cause unreasonable adverse effects to human health or the environment.

C. Comment Relating to New Data

In addition to its comments on the Agency's assessment of existing data, the Panel urged the Agency to review new data form several on-going and recently completed studies. Specifically, the SAP recommended that a full set of details be obtained and evaluated concerning new oncogenicity studies conducted by Leuschner et al. (1979) with 2,4,5-T containing less than 0.05 ppm TCDD and by the National Cancer Institute [NCI] (1979) with TCDD. Also, the SAP recommended similar measures for Dr. James Allen's on-going reproductive toxicity study in monkeys fed a diet containing 25 ppt TCDD (Allen, 1979).

This recommendation is fully consistent with the Agency's customary practice of evaluating new information as part of its continuing review of risks and benefits of registered chemicals. The Agency will review and assess these and any other available studies in the context of the proposed 6(b)(2) hearings.

In conclusion, the Agency has determined that the SAP comments do not warrant a change in the Agency's risk analysis for the non-suspended uses 2,4,5-T and silvex at this time.

III. Issues Relating to Benefits

In the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, the Agency provided a preliminary benefits analysis and acknowledged that further review of the chemical alternatives was necessary before the Agency could make a final assessment of the risks and benefits associated with the continued uses of 2,4,5-T and silvex. Throughout the review of 2,4,5-T and silvex, the Agency has expressed concern about the quality and completeness of much of the data it has obtained on the economic benefits of 2,4,5-T and silvex.

In its response to the Agency's proposal, USDA agreed that these data gaps can best be addressed through a 6(b)(2) hearing for the non-suspended uses of 2,4,5-T and silvex. USDA did not provide substantive comment on the benefits determinations which were presented in the Position Documents. In addition, USDA stated its intention to continue assembling additional data to be submitted to the Agency on the uses of, and benefits associated with, these herbicides. The Agency is also continuing to gather benefits information from other sources.

In conclusion, the USDA's comments on the Agency's preliminary benefits analysis for the non-suspended uses of 2,4,5-T and silvex wholly support the Agency's determination that further review is necessary and can best be addressed through a 6(b)(2) hearing.

IV. Conclusion

The SAP's assessment of the scientific data on the reproductive and the oncogenic effects of 2,4,5-T, silvex, TCDD in test animals is generally consistent with the Agency's position. Also, consistent with the Agency's current efforts were several SAP recommendations for obtaining additional data.

The Panel concluded that it had found no evidence of an "immediate or substantial hazard" to human health or the environment associated with the non-suspended uses, and is likewise the Agency's position. Upon finding evidence of an "imminent hazard", the Agency acts to suspend the pesticide uses which are implicated. An example of such action is the recent emergency action suspending certain uses of 2,4,5-T and silvex.

As was discussed in the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3 for the non-suspended uses, the Agency recommends holding a hearing, in part because the available data indicates that these uses appear to have unreasonable adverse effects on the environment. However, the Agency did not act to suspend these uses as it would have done if it had found an imminent hazard.

The SAP disagreed with the Agency's proposal to hold a hearing and recommended that the Agency not hold a 6(b)(2) hearing at this time. The Agency has taken the Panel's recommendations into account but has decided that such a hearing is appropriate, based on (1) information showing that the non-suspended uses of 2,4,5-T and silvex appear to cause unreasonable adverse effects on man or the environment, (2) the Agency's and the SAP's conclusion that more information is necessary to resolve the issues involved, and (3) that a combined hearing is the most efficient and effective way to resolve the issues.

The Agency holds that it is in the public interest to combine the hearing for the nonsuspended uses with the cancellation hearing for those uses that were suspended on February 28, 1979. Not only will this action be administratively convenient for the Agency, registrants, and interested parties, entailing more efficient use of resources, but it will also ensure that the Agency's concerns on all uses of 2,4,5-T and silvex are addressed consistently.

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Appendix A

In response to comments expressing confusion about the Agency's pasture and range definitions, the Agency is taking this opportunity to correct an inadvertant error in the pasture definition and to modify the range definition.

In the pasture definition the word "and" was inserted in the list of cultural practices in place of the intended word "or" (44 FR 15874; 44 FR 15897, March 15, 1979). Therefore, the definition should be corrected by the substituting of the word "or" for "and" so that the definition now reads as follows:

Pasture is defined as land producing forage for animal consumption, harvested by grazing, which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application *or* other similar practices applied to it. Fencerows enclosing pastures are included as part of the pasture.

This correction clearly specifies that annual application of any one or more of these cultural *practices will classify the land* as pasture.

The following modification of the range definition will further explain the distinction between range and pasture. These modifications are based on the same USDA Forest Service material which was the source for EPA's definition of pasture and range. With these modifications, range is now *defined as follows:*

Range is non-pasture grazing land producing forage from native plant species or introduced species managed as native species. Grazing land which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application, or other similar practices applied to it is excluded. However, forest,[1] as defined in 44 FR 15893, March 15, 1979, are excluded.

Appendix B—Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Scientific Advisory Panel

Review of Notices of Intent To Hold FIFRA Section 6(b)(2) Hearing on 2,4,5-T and Silvex

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel has completed review of the Notices of Intent by the Environmental Protection Agency (EPA) to hold hearings under the provisions of FIFRA Section 6(b)(2) to consider appropriate regulatory action for those uses of 2,4,5-T and Silvex which were not included in the recent suspension orders. The review was completed in open meetings held in Arlington, Virginia, during the periods August 15–16, 1979, and September 20, 1979.

Maximum public participation was encouraged by the Scientific Advisory Panel to ensure an objective and adequate consideration of all relevant scientific issues relating to health and the environment. Public notice of the meetings was published in the **Federal Register** on July 27, 1979, and September 4, 1979. In addition, telephonic calls and special mailings were also sent to the general public who had previously expressed an interest in activities of the Panel.

Written statements relative to 2,4,5-T and Silvex were received from Dow Chemical Company, and Michigan State University.

In addition, oral comments were received from Dr. J. R. Allen, University of Wisconsin Medical School; EPA technical staff; representatives of the Texas State Department of Agriculture; Dow Chemical Company; and the Environmental Defense Fund.

The FIFRA Scientific Advisory Panel wishes to recognize the excellent cooperation and assistance of numerous EPA technical staff thoughout the review of 2,4,5-T and Silvex.

In consideration of all matters brought out during the meeting and careful review of all documents submitted by the Agency and other parties, the Panel unanimously submits the following report:

In response to the Agency's request for advice concerning whether a FIFRA Section 6(b)(2) hearing should be held to resolve questions relative to the continued use of 2,4,5-T and Silvex on rice, rangeland, orchards, sugar cane, and certain non-crop sites, (1) *the Scientific Advisory Panel recommends that the Agency not hold such a meeting at this time.* After extensive review of the data we find no evidence of an immediate or substantial hazard to human health or to the environment associated with the use of 2,4,5-T or Silvex on rice, rangeland, orchards, sugar cane, and the non-crop uses specified in the decision documents.

The Scientific Advisory Panel has extensively reviewed the animal toxicity test data base for teratogenesis, carcinogenesis, and reproductive effects for 2,4,5-T, Silvex, and TCDD and has identified some additional data needs which should be addressed prior to final decision making relative to the safety evaluation of 2,4,5-T and Silvex. (2) *The Scientific Advisory Panel recommends specifically that the full details be obtained and evaluated for the following three studies which were discussed briefly at the hearing:*

1. The oncogenicity study on commercial 2,4,5-T being conducted in Germany in the Laboratorium Fur Pharmakologie Und Toxikologie. An oncogenic study has recently been completed on 2,4,5-T which was specially purified to contain a low concentration of TCDD. However, data is needed on the oncogenicity of commercial 2,4,5-T containing TCDD (≦0.05 ppm).

2. The oncogenicity study recently completed at NCI with TCDD in both rats and mice; and

3. The reproductive toxicity study being conducted at the University of Wisconsin by Dr. Allen in which monkeys are being fed a diet containing TCDD at 25 ppt.

The Scientific Advisory Panel has also reviewed the available data regarding potential human exposure to 2,4,5-T and Silvex from use on rice, rangeland, orchards, sugar cane, and other non-crop applications and the monitoring data related to these uses and would characterize these as incomplete and preliminary in nature. (3) *We therefore recommend that monitoring data be obtained regarding the levels of 2,4,5-T and Silvex and TCDD in milk, and that additional data be gathered regarding the levels of these agents in the tissues of range animals and that information be obtained regarding the levels of these agents in edible aquatic organisms.* . . . In these additional monitoring studies special emphasis should be placed on TCDD levels rather than levels of 2,4,5-T and Silvex, *per se.*

In regard to the specific issues and questions posed by the Agency to the Panel regarding review of 2,4,5-T and Silvex, the Scientific Advisory Panel offers the following responses:

[1] *Lands capable of growing 20 cubic feet of wood* per acre per year of desirable species which are not withdrawn for non-timber purposes.

Issues on Toxicology

Question 1. EPA has found that 2,4,5-T, Silvex, and TCDD are teratogens. Does the Panel agree?

Response: The Scientific Advisory Panel agrees with the Agency that 2,4,5-T, Silvex, and TCDD are teratogens.

Question 2. EPA has found that 2,4,5-T, Silvex, and/or TCDD are fetotoxins. Does the Scientific Advisory Panel agree?

Response: The Scientific Advisory Panel agrees with the Agency that 2,4,5-T, Silvex, and TCDD produce reproductive (fetotoxic) effects.

Question 3. EPA has determined that TCDD exhibits fetotoxic effects and that a No Observable Effect Level (NOEL) has not been established for this effect. Does the Scientific Advisory Panel agree with this finding?

Response: The Panel agrees with the Agency that a NOEL has not been established for TCDD in chronic studies in monkeys. In contrast to the Agency position, the Panel concludes that a NOEL has been established for TCDD for both rats and mice. The Scientific Advisory Panel would like to point out in this regard that the Agency position is relatively close to that of the scientists from the Dow Chemical Company. The Scientific Advisory Panel believes that the dose of 0.001 ug/kg/day is for all practical purposes a NOEL (For the purposes of risk calculation; See Appendix I). It should be pointed out that a NOEL for reproductive effects has been established for commercial 2,4,5-T in all species tested including monkeys.

Question 4. EPA has found that TCDD is carcinogenic in test animals, and thus is a potential human carcinogen. Does the Scientific Advisory Panel concur with this finding?

Response: The Scientific Advisory Panel agrees with the Agency opinion that TCDD is carcinogenic in test animals and therefore may be a potential human carcinogen.

Question 5. EPA has found that TCDD is an extremely potent animal carcinogen. Does the Scientific Advisory Panel agree with this finding?

Response: Answered in question 4 above.

Issues on Exposure

Question 1. EPA believes that human exposure from the use of 2,4,5-T and Silvex on rice may be broad and substantial due to herbicide drift during and after application, and that more diffuse exposure is possible through the water environment and through crayfish, catfish and other food sources. How would the Panel characterize the exposure potentials and concerns for rice use? What questions do they have and how would they be answered by the proposed monitoring plan?

Response: The Scientific Advisory Panel agrees that exposure to 2,4,5-T and Silvex from use on rice may be possible through the water environment and through edible aquatic organisms and other food sources. However, the Scientific Advisory Panel believes that insufficient data was presented or made available to the Panel in support of the argument that human exposure from spray drift and the water environment is likely to be broad or substantial. The questions regarding proposed monitoring have already been addressed. In addition to the need for more data on the concentrations of Silvex, 2,4,5-T, and TCDD in crayfish and catfish, monitoring data should also be obtained on soil sediments.

Question 2. EPA believes that drift from the use of 2,4,5-T/Silvex products on rangeland creates a lower, yet-still-real, potential for exposure due to lower population densities and distribution in range areas relative to rice growing areas. Sparsity of surface water and extreme depth of ground water in many areas would suggest a minimal exposure from aquatic sources used as food. However, beef monitoring shows low levels of dioxin in a limited number of samples from beef that grazed on 2,4,5-T treated range. How would the Panel characterize the exposure potential and concerns for the use of these chemicals on range? What unanswered questions do they believe the Agency should address in determining exposure potential?

Response: The Scientific Advisory Panel agrees with the Agency that there is a potential for exposure as a result of drift from the use of 2,4,5-T and Silvex products on rangeland and that the potential for exposure from this mechanism would be lower than that from use of the agents on rice. However, the Panel believes that the data made available to the Panel did not provide a convincing argument for the existence of an immediate or substantial hazard from the use of Silvex and 2,4,5-T on rangelands.

Question 3. Little is known about the potential for dietary exposure to Silvex and/or TCDD from the uses of Silvex on food crops, except for apples on which Silvex residues have been detected. Given the nature of the contaminant TCDD, EPA has reason for presuming that exposure to food consumers and the environment is possible from these uses. What are the Panel's views on the potential for ingestion exposure from these uses?

Response: Although there is information on the use patterns of Silvex in orchard crops, the Scientific Advisory Panel believes sufficient residue data is not currently available for a definitive opinion on dietary exposure to Silvex.

Question 4. The Agency believes that TCDD and 2,4,5-T move in water from rice to other environmental compartments thereby increasing exposure to widely diffuse populations. Does the Scientific Advisory Panel concur with this?

Response: The Panel agrees with the Agency that it would be possible for 2,4,5-T to move in water from rice fields to other environmental compartments and to thereby increase exposure to widely diffuse populations. However, we believe such movement would be unlikely for TCDD.

General Issues

Question 1. Do the residues (2,4,5-T, Silvex and TCDD) in water, sediment, aquatic organisms and/or the potential for exposure from herbicide drift, in light of the toxicological attributes of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No. (See recommendation (1).)

Question 2. Can the Scientific Advisory Panel assess whether the residues being found in the rice areas are due to the rice use or to other previously permitted uses?

Response: The Panel is not aware of data sufficient to answer this question. (See recommendation (3).)

Question 3. Do the exposure potentials in range use, in light of the toxicological characteristics of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No. (However, see recommendation (3).)

In consideration of the potential toxicity of TCDD, (4) *the Scientific Advisory Panel recommends that efforts should be made to further reduce the level of chemical TCDD in commercial preparations of 2,4,5-T and Silvex.*

Dated: September 26, 1979.

For the Chairman.

Certified as an accurate report of findings.

H. Wade Fowler, Jr.,

Executive Secretary, FIFRA Scientific Advisory Panel.

Appendix I—The FIFRA Scientific Advisory Panel Evaluation of the Oncogenicity, Fetotoxity, and Exposure Characteristics for 2,4,5-T, Silvex and TCDD

Introduction

In our opinion the major health and environmental issues relative to possible regulatory action by the Agency center around the potential of commercial forms of 2,4,5-T and Silvex contaminated with TCDD to pose carcinogenic, teratogenic and reproductive risks to persons as a result of (1) exposure during mixing and application, or (2) direct exposure to the spray as a result of living in the immediate area of application. In contrast, the major concern relative to TCDD, essentially free of 2,4,5-T or Silvex, arises from the degree to which this agent concentrates in portions of the human food chain. The primary concern of the Scientific Advisory Panel is the potential carcinogenic, reproductive, and teratogenic risk from use of commercial 2,4,5-T and Silvex contaminated with TCDD. The potential for these same risks from TCDD essentially free of 2,4,5-T and Silvex is of secondary concern, as is the potential risk posed by 2,4,5-T or Silvex essentially free of TCDD.

Commerical 2,4,5-T

Oncogenicity. Seven studies of variable quality have been carried out in mice to examine the oncogencity of commercial 2,4,5-T contaminated with TCDD. The results of these studies have not demonstrated a carcinogenic risk from commercial 2,4,5-T in this rodent species. A complete study of the carcinogenic potential of commercial 2,4,5-T contaminated with TCDD at ≦0.05 ppm has not yet been reported in rats. However, such a study has recently been completed by the Laboratorium for Pharmkologie und Toxikologie, Hamburg, Germany. The Scientific Advisory Panel was informed during the recent meeting that gross autopsy examination of these animals revealed no increase in tumors relative to the control groups. However, until the pathological examination is complete no definitive conclusion can be drawn relative to the oncogenic potential of commercial 2,4,5-T in rats. The Dow Chemical Company has recently completed a study of the oncogencity of a specially purified sample of 2,4,5-T in rats. This sample of 2,4,5-T contained less than 0.0003 ppm TCDD. In this study there was no increase in tumors resulting from exposure to this purified

preparation of 2,4,5-T fed at the maximum tolerated dose (30 mg/kg/day) or at lower doses (10 mg/kg/day and 3 mg/kg/day). Thus it appears that 2,4,5-T, which is essentially free of contaminating TCDD, is not oncogenic in rats. However, this study is of limited predictive value since the form of 2,4,5-T of concern to the Scientific Advisory Panel is commercial 2,4,5-T; in other words, 2,4,5-T contaminated with TCDD.

Chronic tests carried out using TCDD free of 2,4,5-T have demonstrated that TCDD is carcinogenic in rats and carcinogenic or tumorigenic in mice. Thus, since commercial 2,4,5-T contains TCDD as a contaminant (≦0.05 ppm) the lack of a carcinogenic response in rodents using commercial 2,4,5-T must be viewed with caution. The Scientific Advisory Panel is of the opinion that some carcinogenic risk to man is posed by exposure to 2,4,5-T contaminated with TCDD at the level present in the 2,4,5-T in current use. However, the data currently available indicate that this risk is not substantial.

In summary, the evidence currently available indicates there is not an immediate or substantial oncogenic risk to man from exposure to 2,4,5-T contaminated with TCDD at a level of ≦0.005 ppm.

Reproductive and Embryo Toxicity

Commercial 2,4,5-T produces fetal toxicity and is teratogenic in rats and mice. According to the data presented to the Scientific Advisory Panel during the August 15–16, 1979 meeting, the no effect level for embryo toxicity for commercial 2,4,5-T in various species when examined in conventional toxicity studies is as follows: rat, 25 mg/kg/day; mouse, 20 mg/kg/day; hamster, 40 mg/kg/day; and monkey, 40 mg/kg/day. However, a recent study conducted at the National Center for Toxicological Research revealed teratogenic effects in A/J mice at the lowest dose of commercial 2,4,5-T tested (15 mg/kg/day). It would appear, therefore, that there are strain differences in the no effect level for 2,4,5-T in mice.

Two three-generation studies of 2,4,5-T reproductive toxicity have been carried out in rats. One of these studies was carried out using commercial 2,4,5-T containing ≦0.05 ppm TCDD. No teratogenic effects, reproductive toxicity or fetal toxicity were observed in any animals at the doses tested (3, 10 and 30 mg/kg/day). In contrast another three-generation study carried out using purified 2,4,5-T (≦0.0003 ppm TCDD) reported a significant decrease in neonatal survival at 10 and 30 mg/kg/day but not at 3 mg/kg/day. However some effects suggestive of reproductive toxicity were noted at the intake level of 3 mg/kg/day in this study. The Scientific Advisory Panel believes that this three-generation study establishes for practical purposes a NOEL and recommends that this NOEL be used for subsequent evaluation of risk.

In summary, the Scientific Advisory Panel believes that these data suggest that a potential for reproductive risk and embryo toxicity exists for persons engaged in the mixing and application of commercial 2,4,5-T. However, with use of protective clothing such as a one piece jump suit with long sleeves, gloves and, perhaps, respirators, risks should be reduced to an acceptable level. The potential for significant reproductive and teratogenic risk to persons living in the immediate area of the spraying operations does not appear to be substantial except as they may be directly exposed on a chronic basis.

The Panel has some reservations relative to the validity of the three-generation study in rats carried out by the Laboratory fur Pharmakologie and Toxikologie using commercial 2,4,5-T (≦0.05 ppm TCDD), and recommends that an additional three-generation study in rats using commercial 2,4,5-T be carried out.

Silvex

Oncogenicity. The carcinogenic testing of commercial Silvex has been less extensive than with 2,4,5-T. However, those few studies which have been carried out did not indicate an increase in oncogenicity as a result of chronic exposure to Silvex. Although no carcinogenic risk has been demonstrated with commercial Silvex, these data must be viewed with some caution because of the contamination of commercial Silvex with TCDD.

Reproductive and Embryo Toxicity. In contrast to commercial 2,4,5-T, very few studies of the reproductive toxicity of Silvex have been carried out. Those studies with commercial Silvex that have been carried out in rats and mice indicate that commercial Silvex is teratogenic in mice at high doses (400 mg/kg/day). Silvex is also fetotoxic in mice and rats and the no effect level in rats is 25 mg/kg/day.

Thus commercial Silvex does appear to pose some risks to reproduction and fetal viability. Much less information is available concerning the degree of exposure of humans to Silvex during mixing and spraying operations than is the case with 2,4,5-T. However, it should also be possible using proper protective clothing to reduce the reproductive and teratogenic risk from commercial Silvex to an acceptable level. Similarly there does not appear to be any substantial risk to persons living in the immediate area of the spraying except from direct exposure on a chronic basis.

TCDD

Oncogenicity. Two major studies of the oncogenicity of TCDD have been reported. One study in rats has been carried out by the Dow Chemical Company and another in mice was performed by the Research Institute of Oncopathology in Hungary. A third study in mice and rats has recently been completed by NCI, but the results of this study were not yet available.

There was an increase in tumors of the liver, lung and hard palates/nasal turbinates in the rats fed of 0.1 μg/kg/day of TCDD in the diet. At a dose of 0.01 μg/kg/day there was an increase in hyperplastic nodules in the livers of the female rats. The EPA Carcinogen Assessment Group (CAG) has concluded that this increase in hyperplastic nodules at the dose of 0.01 μg/kg/day indicates that TCDD is also carcinogenic at this dosage level. The Scientific Advisory Panel concludes that there is a tumorigenic response at 0.01 μg/kg/day but has reservations as to whether hyperplastic nodules are precursors, *per se*, to hepatocellular carcinoma. (See Appendix II)

An increased incidence of liver tumors were produced in studies in male outbred Swiss mice in which TCDD was given by gavage at a dose of 0.7 μg/kg/week for one year. However, in this study there was no significant increase in tumor formation in animals given TCDD at 7.0 μg/kg/day although there was a decreased life span in the mice receiving this dose. There was also no increase in tumors in animals given TCDD at a dose of 0.007 μg/kg/week. Evaluation of this study by the Scientific Advisory Panel is difficult, since the type of liver tumor produced was not identified. Although the authors stated that the ratio of benign hepatomas to hepatocellular carcinomas was the same in the animals receiving the 0.7 μg/kg/week dose of TCDD as in the controls, it is not clear whether there was a significant increase in hepatocellular carcinomas in the treated animals.

The Scientific Advisory Panel concludes that there is a level of TCDD below which no oncogenic or tumorigenic effects were seen in either mice or rats. The dose level for tumorigenic response in the outbred strain of Swiss mice used in the Hungarian oncogenic study lies between 0.007 and 0.7 μg/kg/week. The Scientific Advisory Panel believes that the data available from this study are insufficient to reach a firm conclusion regarding whether there was a true oncogenic response in mice. In rats there was some controversy over which level of exposure to TCDD demonstrated an oncogenic effect. The Dow Chemical Company scientists stated that the level at which no oncogenic effects are seen lies between a dose of 0.1 and 0.01 μg/kg/day in the diet. The EPA Carcinogen Assessment Group concluded that the non-oncogenic dose lies between 0.01 and 0.001 μg/kg/day. Thus, there was agreement concerning the lack of an oncogenic response at the dose level of 0.001 μg/kg/day TCDD.

The major concern of the Scientific Advisory Panel relative to the potential oncogenic risk from TCDD is whether TCDD accumulates in the human food chain. The data necessary to evaluate this risk must be derived from monitoring data for TCDD itself. The oncogenic risk from TCDD present as a contaminant in commercial 2,4,5-T and Silvex is best determined in those experiments in which commercial 2,4,5-T or Silvex contaminated with TCDD has been administered chronically to rats and mice.

The monitoring data obtained thus far does not suggest that TCDD derived from commercial 2,4,5-T and Silvex exhibits any tendency to accumulate in the human food chain in amounts which would pose a substantial risk. For example TCDD has been detected in some fat samples from cows grazed on rangeland immediately after spraying with commercial 2,4,5-T and sacrificed 2 weeks later. If one assumes that all beef fat in the U.S. contains TCDD at the level found in these studies (approximately 10 ppt) and if one assumes further that the average level of beef intake in the U.S. population is 6% of the diet; (1.5 kg food/day; 15% of beef is fat) and produces a 22% incidence of tumors at 0.1 μg/kg/day (Dow Study) a risk of 4×10^{-6} can be calculated. It should be pointed out that this is an extreme worse case calculation since the present data indicate that only a small percent (approximately 7%) of beef fat samples from animals fed on ranges immediately after spraying with 2,4,5-T containing TCDD and that all beef eaten in the U.S. does not come from ranges sprayed with 2,4,5-T (only 2%). Thus, although it appears that there is some

potential oncogenic risk from TCDD present in the food chain, on the basis of the current monitoring data, the risk is judged to be small.

Reproductive Toxicity. The results of the embryo toxicity studies indicate that the no effect level for TCDD in mice is 0.1 μg/kg/day (days 6–15 of gestation), in rats is 0.03 μg/kg/day (days 6–15 of gestation), and in monkeys is 0.02 μg/kg/3 times per week (days 20–40 of gestation).

In a three-generation reproductive study carried out in rats by the Dow Chemical Company clear cut embryo toxicity was seen at doses of 0.1 and 0.01 μg/kg/day of TCDD. At the dose of 0.001 μg/kg/day there was a decreased gestational survival in the F_1 generation but not in earlier or later generations. Postnatal survival in the group receiving 0.001 μg/kg/day was decreased in the F_{1a} generation and increased in the F_{1b} generation relative to the controls. An increase in dilated renal pelvis was also seen in the F_{1a} and F_{1b} generation in the animals receiving 0.001 μg/kg/day but not in later generations or at the 0.01 μg/kg/day dose. Although these effects at 0.001 μg/kg/day are suggestive of an embryo-toxic effect, the inconsistency of the effects from generation to generation and in relation to the higher dose of 0.01 μg/kg/day (dilated renal pelvis) suggests that the 0.001 μg/kg/day dose is for all practical purposes a no effect level.

Long term studies in monkeys have shown reproductive toxicity from TCDD at levels of 50 ppt in the diet. Studies are currently underway at 25 ppt of TCDD in the diet, but results are not yet available. An intake of TCDD of 50 ppt in the diet is equivalent to approximately 0.002 μg/kg/day. If no reproductive toxicity is seen in the monkeys exposed to TCDD in the diet at 25 ppt, then the no effect level in the monkey will be similar to that seen in the rat, namely about 0.001 μg/kg/day.

The major concern of the Scientific Advisory Panel relative to the potential reproductive toxicity or teratogenic effects of TCDD is whether it accumulates in human food chains as previously noted for the oncogenic potential of TCDD. The reproductive toxicity and teratogenic potential of TCDD present as a contaminant in commercial 2,4,5-T and Silvex is best determined from experiments in animals exposed to commercial 2,4,5-T or Silvex contaminated with TCDD.

If one assumes the worse case situation described previously in the evaluation of the oncogenic risk from TCDD in which TCDD is proposed to be present in the fat of all cows marketed in the U.S., the maximum intake would be approximately 2×10^{-6} μg/kg/day. Using a 0.001 μg/kg/day as the no effect level the safety factor would be approximately 500. As pointed out previously in the section on the oncogenicity of TCDD, this calculation represents an extreme exaggeration of exposure to TCDD. The Scientific Advisory Panel believes, therefore, that the current monitoring data do not indicate that there is a substantial reproductive or teratogenic risk posed by the accumulation of TCDD in the human food chain.

Appendix II—A Selected Review of the Histology of the Dow TCDD Study (Tox. Appl. Pharm. 46, 279 (1978))

Drs. Donna Kuroda, Richard Kociba and I reviewed 3 representative microscopical sections each from control, 0.01, and 0.1 μg/kg/day level TCDD exposed female Sprague Dawley rats. These sections were selected by Dr. Kociba to demonstrate hyperplastic nodules and lesions designated hepatocellular cancers (see Table #5 R. J. Kociba et al. Tox. & Appl. Pharm. *46*, 279 (1978)). Control sections were used for comparison.

Control animals, selected from timed sacrifices, showed a general presentation of the liver architecture. A natural incidence (spontaneous?) of extramedullary hematopoiesis, bile duct reduplication, and "hyperplastic nodules" was found by Dr. Kociba (Table 5) and demonstrated in the sections provided to me. Kociba and colleagues considered a tissue mass to represent a hyperplastic nodule if a group of liver cells, with or without sinusoidal lining cells, formed a discrete population with cellular structure and/or tinctorial properties different from the surrounding parenchyma. These growths may or may not cause compression of surrounding parenchyma and may or may not have bile duct formation. Sharp demarcation from the surrounding parenchyma was observed.

In addition, there were both acute inflammatory exudates and granuloma-like lesions in the controls, not associated with the hyperplastic nodule. In addition there appeared to be an acute cholangitis. No evidence of fibrosis was present.

Sections from the high dose exposure animals (0.1 μg/kg/day) showed some distortion of the hepatic parenchyma with cellular variability and thickening of the liver cell plates. Portal tracts were sometimes associated with dense collections of lymphocytes. Prominent were hyperplastic nodules and lesions characterized by Kociba and associates as hepatocellular carcinomata. These latter lesions showed more marked cellular differences from surrounding parenchyma and from hyperplastic nodules. In general, the liver cell nuclei were larger occupying a greater portion of the cell volume, the cell plates more disordered, formation of acinar and tubular forms were identified, and no formation of portal tracts were present in these lesions. These masses in one instance, arose in a hyperplastic nodule. No defined microscopical or gross evidence of invasion of the neoplastic cells into adjacent tissues was noted either at autopsy (according to Kociba) or by microscopy. Not infrequently fat was present in hyperplastic nodules but not in the "carcinomata."

The parenchyma adjacent to the carcinomatans and hyperplastic nodules showed some cellular irregularity, staining variation, and hyaline intracytoplasmic masses. No significant evidence of increased inflammatory exudates or fibrosis was noted, but bile duct reduplication was present.

The midrange dose shows hyperplastic nodules, the remaining changes were identical with the high dose, but these slides did not show a carcinoma. I believe that the group at Dow extensively and properly surveyed the evidence of hepatocellular disease following exposure of rats to TCDD. Autopsies on animals were conducted by pathologists and tissue sections were selected by them. Their microscopial review was extensive. Their nomenclature was defined and understandable. I personally would have been more conservative than they in designating carcinomata, so their result is a "worst case" designation. From these discussions and reviews, I am very comfortable with their evaluation for toxic injury and carcinogenesis. Additionally, I believe liver cancer was shown in the high dose level; might be questioned in the midrange level, but was not present in the low dose group.

Edward Smuckler,

Professor and Chairman, Department of Pathology, University of California School of Medicine, San Francisco, Calif.

August 15, 1979.

Survey conducted at EPA Headquarters, 401 M Street SW., Washington, D.C. 20460.

Appendix C—Department of Agriculture, Office of the Secretary

August 10, 1979.

Mr. Edwin L. Johnson,

Deputy Assistant Administrator for Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. 20460.

Dear Ed: The Secretary has asked me to respond to your letter of July 9, 1979, regarding the proposal to hold hearings under Section 6(b)(2) of the Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. 136d(b)(2) to determine whether or not the nonsuspended uses of 2,4,5-T and silvex should be cancelled.

As you know, the Secretary is a party in the Section 6(b)(1) hearing. Except for slightly different use patterns and exposure considerations, the issues on both the suspended and nonsuspended uses are similar and we, therefore, plan to participate in the 6(b)(2) portion as well.

Contrary to statements in the Notice of Intent to hold a hearing on the remaining uses of silvex, the Department of Agriculture has not provided information on the "social, economic, and environmental benefits" of using silvex to you. This information is currently being collected by the joint USDA/States/EPA assessment team, but since an RPAR notice was not issued on this compound, the team, which was organized recently, has only had time to develop some preliminary data.

We agree that it is in the best interest of everyone to attempt to resolve all issues in a consolidated hearing. We are preparing to have information available on all uses of both 2,4,5-T and silvex for presentation to the Administrative Law Judge during these proceedings.

We will be submitting for the record of the hearings the benefit and exposure information contained in the 2,4,5-T assessment report prepared by the joint USDA/States/EPA assessment team as well as information presently being gathered by the joint assessment team on silvex. We believe that the assessment team activity has

been an effective means for assembling information needed in the regulatory decision process.

Your notice indicates that additional data on the benefits of the non-suspended uses of 2,4,5-T will be needed before a final regulatory decision can be made. It would be most helpful to us and to the process if you would point out specifically where the data in the USDA/States/EPA report "The Biologic Economic Assessment of 2,4,5-T" is not adequate. We are anxious to cooperate with you in filling any data gaps that may exist to assure that all possible information can be examined in reaching a final decision.

Sincerely,

Barry R. Flamm,

Director, Office of Environmental Quality.

[FR Doc. 79-38026 Filed 12-12-79; 8:45 am]

BILLING CODE 6560-01-M

[FRL-1373-8; OPP-30000/31A]

Final Determination Concerning the Rebuttable Presumption Against Registration for Certain Uses of Pesticide Products Containing Silvex; Intent To Hold a Hearing To Determine Whether or Not Certain Uses of Silvex Should Be Canceled; Publication of Final Position Document Concerning All Non-Suspended Uses of Silvex

AGENCY: Environmental Protection Agency.

ACTION: Final notice of intent to hold a hearing concerning all non-suspended uses of pesticide products containing 2-(2,4,5-trichlorophenoxy) propionic acid (silvex) to determine whether or not such uses should be cancelled, and announcement of findings concerning the risks and benefits associated with such uses of silvex products.

SUMMARY: On July 9, 1979, EPA announced its preliminary determination concerning the Rebuttable Presumption Against Registration (RPAR) review of all uses of pesticide products containing 2-(2,4,5-trichlorophenoxy) propionic acid (silvex) not suspended by prior Agency action, and proposed to hold a hearing to determine whether or not these uses of silvex should be cancelled. See 44 FR 41536, July 17, 1979 (The "Preliminary Notice"). Pursuant to Sections 6(b) and 25(d) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), copies of related decision documents were forwarded to the Secretary of Agriculture and the FIFRA Scientific Advisory Panel for comment.

This notice constitutes the final determination concerning the RPAR review for all non-suspended uses of silvex. The Agency has determined that the potential oncogenic, fetotoxic, and teratogenic risks associated with these uses do not appear to be justified by offsetting economic, social, or environmental benefits and that such uses therefore appear to cause "unreasonable adverse effects on the environment," as defined by FIFRA Section 2(bb). The Agency has also determined that there are uncertainties in the data concerning the risks and benefits of the non-suspended uses, and that additional data relating to the determination of whether or not to cancel registrations for these uses can be developed for and through a hearing.

Accordingly, this notice (1) announces that the Agency will hold a hearing in accordance with FIFRA Section 6(b)(2) to determine whether or not uses of silvex products which have not been suspended should be cancelled or reclassified, and (2) describes the procedure which should be followed by interested persons who wish to participate in the hearing to be held under Section 6(b)(2).

FOR FURTHER INFORMATION CONTACT: Michael Dellarco, Project Manager, Special Persticide Review Division (TS-791), Environmental Protection Agency, 401 M Street, S.W., Room 447, Washington, D.C. 20460, Telephone (202) 557-8244.

SUPPLEMENTARY INFORMATION: The Agency's final Position Document (PD 4) reviews specific findings concerning the risks and benefits of non-suspended uses of silvex and contains a discussion of the comments of the FIFRA Scientific Advisory Panel and the Secretary of Agriculture on the Agency's preliminary findings and initial proposal to hold a hearing under section 6(b)(2). The PD 4 and the comments of the Scientific Advisory Panel and the Secretary of Agriculture are also published in their entirety in the appendix to this notice.

I. Background

On February 28, 1979, the Administrator of the Environmental Protection Agency ordered emergency suspension of products containing silvex and registered for forestry, right-of-way, pasture, home and garden, ditch bank, aquatic weed control, and commercial/ornamental turf uses, and issued notices of intent to cancel these uses. See 44 FR 15897, March 15, 1979. The emergency suspension of certain silvex uses was based in part on information developed and collected during the Rebuttable Presumption Against Registration (RPAR) review of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) registrations. See 43 FR 17116, April 21, 1978. 2,4,5-T and silvex both contain the extremely toxic chemical 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) as an inadvertant but unavoidable contaminant, have comparable use patterns and correspondingly comparable exposure potential, and may thus present similar risks.

At the time the suspension orders were issued, silvex was a candidate for a rebuttable presumption against registration (RPAR), but an RPAR had not been issued. Following the suspension actions, the Agency conducted an expedited RPAR review of all remaining non-suspended uses of silvex. The non-suspended uses of silvex include rangeland, rice, sugarcane, orchards and non-crop uses.[1] Subsequently, on July 9, 1979, EPA announced its determination concerning the RPAR review of the remaining non-suspended uses of silvex, and proposed to hold a hearing to determine whether or not these uses of silvex should be cancelled. See 44 FR 41536, July 17, 1979. Copies of the Position Document summarizing the Agency's preliminary findings regarding the risks and benefits associated with the non-suspended uses of silvex (PD 1/2/3) and of the Agency proposal to hold a hearing were forwarded to the Secretary of Agriculture and the FIFRA Scientific Advisory Panel for comment, as required by sections 6(b) and 25(d) of FIFRA. Although not required to do so by FIFRA, the Agency also afforded registrants and other interested persons an opportunity to submit comments on the proposed action.

This notice constitutes the Agency's final determination concerning the RPAR review of the non-suspended uses of pesticide products containing silvex and final decision concerning the proposal to hold a hearing under section 6(b)(2) to determine whether or not the remaining uses of silvex should be cancelled. In brief, the Agency has determined that the potential oncogenic, fetotoxic and teratogenic risks associated with these uses of silvex do not appear to be justified by offsetting economic, social, or environmental benefits. Position Document 4, which is included in the appendix to this notice, summarizes the evidence on which this determination is based.

The Agency has also determined that further analysis of the risks and benefits of the non-suspended uses of silvex will enable the Agency to decide whether or not registration of the remaining uses of

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[1] The term "non-crop uses" refers to all other currently registered uses of silvex, including use at the following sites: fences, hedgerows (not otherwise included in suspended uses, e.g., rights-of-way, pasture); industrial sites or buildings (not otherwise included in suspended uses, e.g., rights-of-way, commercial/ornamental turf); storage areas; waste areas; vacant lots; parking areas.

silvex should be cancelled or reclassified, and that pertinent information concerning the risks and benefits of these uses can be assembled and evaluated by holding a hearing pursuant to FIFRA section 6(b)(2). Pursuant to 40 CFR 164.32, the Agency intends to petition the Chief Administrative law Judge to consolidate the hearing initiated by this notice in the cancellation hearing for suspended uses of 2,4,5-T and silvex. It is expected that a consolidated formal evidentiary hearing on cancellation of all silvex registrations will begin early next year.

II. Legal Authority

A. General

In order to obtain a registration for a pesticide under FIFRA, a manufacturer must demonstrate that the pesticide satisfies the statutory standard for registration. That standard requires (among other things) that the pesticide perform its intended function without causing "unreasonable adverse effects on the environment." FIFRA § 3(c)(5). "Unreasonable adverse effects on the environment" is defined 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." FIFRA section 2(bb).

In effect, this standard requires a finding that benefits of each use of the pesticide exceed the risks of that use, when the pesticide is used in accordance with the terms and conditions of registration, or in accordance with widespread and commonly recognized practice. The burden of proving that a pesticide satisfied the registration standard is on the proponents of registration (e.g., registrants or users) and continues as long as the registration remains in effect. Under section 6 of FIFRA, the Administrator is required to cancel the registration whenever he determines that the pesticide no longer satisfies the statutory standard for registration.

B. The RPAR Process

The Agency created the rebuttable presumption against registration (RPAR) process to facilitate the identification of pesticide uses which may not satisfy the statutory standard for registration and to provide a structure for the gathering and evaluation of information about the risks and benefits of these uses. The structure permits public participation at major points in the evaluation process.

The regulations governing the RPAR process are set forth at 40 CFR 162.11. This section provides that a rebuttable presumption shall arise if a pesticide meets or exceeds any of the risk criteria identified in the regulations. After an RPAR is issued, registrants and other interested persons are invited to review the data upon which the presumption is based and to submit data and information to rebut the presumption. Respondents may rebut the presumption of risk by showing that the Agency's initial determination of risk was in error, or by showing that the exposure to man or other sensitive species which is likely to be associated with use of the pesticide will not result in a significant risk of adverse effects of the type in question. Further, in addition to submitting evidence to rebut the risk presumption, respondents may submit evidence as to whether the economic, social and environmental benefits of use of the pesticide subject to the presumption outweigh the risk of use.

The regulations require the Agency to conclude an RPAR by issuing a Notice of Determination in which the Agency states and explains its position on the question of whether the RPAR risk presumptions have been rebutted. If the Agency determines that the presumption has not been rebutted, it then considers information relating to the social, economic, and environmental costs and benefits of use of the pesticide, including information which registrants, the U.S. Department of Agriculture, and other interested persons have submitted to the Agency and other benefits information known to the Agency. If the Agency determines that the risks of a particular pesticide use appear to outweigh its benefits, the Agency may elect to conclude the RPAR process by issuing a notice of intent to cancel, deny, or reclassify registration of the pesticide for the use in question, pursuant to FIFRA sections 6(b)(1) and 3(c)(6), or by issuing a notice of intent to hold a hearing to determine whether or not registration for that use should be cancelled, denied, or reclassified, pursuant to FIFRA section 6(b)(2).

C. Choice of Mode of Action

Two types of proceedings are available under Section 6(b) of FIFRA to cancel a pesticide registration, or to modify the terms and condition of its registration: FIFRA Section 6(b)(1) proceedings and FIFRA Section 6(b)(2) proceedings. In general, FIFRA Section 6(b)(1) proceedings begin with a notice specifying the regulatory action which the Administrator is proposing. This action takes effect automatically, without hearings, at the expiration of a notice period prescribed by statute, unless a registrant or a person adversely affected by the notice requests a hearing within that period. If a hearing is requested, the regulatory action proposed by the Administrator does not take effect; however, at the conclusion of the hearing, the Administrator may implement the proposed action, if he determines that it is appropriate to do so based on the record developed in the hearing.

Section 6(b)(2) proceedings, on the other hand, begin with a general notice specifying the issues which the Administrator desires to have explored at a hearing. Unlike Section 6(b)(1) proceedings, the Section 6(b)(2) proceeding does not include an initial proposed regulatory solution which would take effect automatically if a hearing is not requested. Interested persons may participate in the hearing; at the conclusion of the hearing, the Administrator may take whatever action he deems appropriate, based upon the record developed in the hearing, including cancellation of a pesticide registration or modification of the terms and conditions of its registration.

The judgment of whether to issue a FIFRA section 6(b)(1) or a section 6(b)(2) notice is within the sole discretion of the Administrator (or his duly designated delegatee). If the Administrator determines that the risks of a pesticide use appear to outweigh its benefits, he may issue a notice of intent to cancel pursuant to FIFRA section 6(b)(1). If, however, the Administrator's judgment concerning the risks and benefits associated with a particular pesticide use on the appropriate regulatory response is only tentative, the Administrator may issue a notice under FIFRA Section 6 (b)(2) declaring his intention to hold a hearing "to determine whether or not its registration should be cancelled."

D. External Review

The statute requires the Agency to submit notices to be issued pursuant to FIFRA section 6 to the Secretary of Agriculture, along with an analysis of the impact of the proposed action on the agricultural economy. FIFRA section 6(b). The Agency must submit these documents to the Secretary of Agriculture at least 60 days before issuing the notice in final form. If the Secretary of Agriculture comments, in writing, within 30 days after receiving the notice, the Agency is required to public the Secretary's comments and the Administrator's responses to them along with the notice. FIFRA also requires the Administrator to submit FIFRA section 6 notices, at the same time and under the same procedures as those described above for review by the Secretary of Agriculture, to the Scientific Advisory Panel for comment on the impact of the

action on health and the environment. FIFRA section 25(d).

Although not required to do so under FIFRA, the Agency had determined that it is consistent with the general theme of the RPAR process and the Agency's overall policy of open decisionmaking to afford registrants and other interested persons an opportunity to comment on the bases for the proposed action during the time that the proposed action is under review by the Secretary of Agriculture and the Scientific Advisory Panel. Accordingly, appropriate steps were taken to make copies of Position Document 1/2/3 on the non-suspended uses of silvex available to registrants and other interested persons at the time the preliminary decision documents were transmitted for formal external review, through publication of a notice of availability in the Federal Register, and by other means. Registrants and other interested persons were allowed the same period of time to comment—30 days—that FIFRA provides for receipt of comments from the Secretary of Agriculture and the Scientific Advisory Panel.

The decision to issue a FIFRA section 6 notice is a preliminary determination, pending external review and Agency analysis of comments received. On the basis of these comments, the Agency may withdraw the notice, issue a final notice without modification, or modify the notice, as appropriate.

III. Determinations and Announcement of Regulatory Actions

As detailed in the Preliminary Notice and PD 1/2/3, the Agency considered information on the risks associated with the non-suspended uses of silvex, including information submitted by registrants and other interested persons in rebuttal to the 2,4,5-T RPAR. The Agency also considered information on social, economic and environmental benefits of the non-suspended uses of silvex, including benefits information submitted by the United States Department of Agriculture. The Agency's assessment of the risks and benefits of the non-suspended uses of silvex, its conclusions and determinations that the non-suspended uses of silves appear to cause unreasonable adverse effects on the environment, and its determination that a section 6(b)(2) hearing on these uses is warranted, were set forth in detail in PD 1/2/3. The PD 1/2/3 was adopted by the Agency as its statement of reasons for the determinations and actions announced in the Preliminary Notice of Determination issued on July 17, 1979 (44 FR 41536).

This Notice constitutes the Agency's *Final Notice of Determination* Concerning the RPAR of the non-suspended uses of silvex. It reflects any modifications in the Agency's initial determinations on the risks and benefits of non-suspended pesticide uses which the Agency has concluded are appropriate, after review of the comments and information received concerning PD 1/2/3 and the Preliminary Notice from the Secretary of Agriculture, the SAP and any other sources. This Notice also indicates that there is no modification of the regulatory action announced in the Preliminary Notice.

PD 4, which accompanies this Notice, discusses in detail the comments that were received from the SAP and the Secretary of Agriculture,[2] the Agency's response to these comments, and the Agency's reasons for changing or not changing its initial determinations and the regulatory action announced in the Preliminary Notice. Finally, this Notice announces the regulatory action which the Agency is implementing concerning silvex. The Agency hereby incorporates PD 1/2/3 and PD 4 as its statement of reasons for this action.

A. Determination on Risks

In the Preliminary Notice, the Agency announced its determination that silvex and/or silvex's TCDD contaminant meet or exceed the risk criteria at 40 CFR 162.11(a) for carcinogenic, fetotoxic, and teratogenic effects, and that the rangeland, rice, sugarcane, orchard and non-crop area uses of silvex pose risks of these adverse effects to human populations. The Agency has determined that information available to it (including information submitted to rebut these risk criteria for the 2,4,5-T RPAR) is insufficient to lay to rest the Agency's concerns that silvex and/or TCDD pose risks of fetotoxic and teratogenic effects in unborn children, and that TCDD and silvex containing TCDD pose risks of cancer among exposed populations. The Agency has determined that the non-suspended uses of silvex create opportunities for human exposure to these chemicals and that such exposure appears generally to cause adverse human effects.[3] The Agency has therefore concluded that the oncogenic, fetotoxic and teratogenic risks associated with the non-suspended uses of silvex are of sufficient magnitude to require the Agency to determine whether the non-suspended uses of silvex offer social, economic, or environmental benefits which offset these risks.

B. Determination of Benefits

The uses of silvex which are subject to this notice fall into five categories: range, rice, sugarcane, orchard and non-crop areas. For each of these use categories an estimate of the economic impact of cancellation of silvex was made.[4] These estimates are intended only as approximations based on available information.[5] The Agency's analysis of this available information leads to the conclusion that the benefits of silvex for the five categories of uses are approximately as set forth below.

(1) *Rangeland.*[6] There are an estimated one billion acres of range and pasture land suitable for grazing in the contiguous 48 states, plus 351 million acres in Alaska and 3 million acres in Hawaii. About 90 percent of this total acreage is rangeland. Of this total, approximately one percent is treated with herbicides, primarily 2,4-D. Only about 150,000 acres, or less than 0.1% of range acres, are treated with silvex.

Silvex is used to control various woody and herbaceous plants found in rangeland. Most silvex use is directed at control of various oak species which compete with desirable forage plants for water, nutrients, sunlight and space.

[2] The comments from the SAP and the Secretary of Agriculture are attached as appendices to PD 4. All other comments are available in the 2,4,5-T public file for inspection and review.

[3] The Agency is continuing to collect and review new laboratory data on the toxic effects of these chemicals in animals, and monitoring data on residues of these chemicals in environmental media.

[4] It is assumed that 2,4,5-T also would be cancelled and unavailable as a substitute for silvex in view of the virtually identical toxicological characteristics of the two compounds and the similarity of their benefits. It is unlikely that one one of them would be cancelled for the uses for which they are alternatives for each other.

[5] The Agency is continuing to collect and review data relating to the benefits of silvex for range, rice, sugarcane, orchard, and non-crop areas.

[6] In response to comments expressing confusion about the Agency's range and pasture definition, provided in PD 1/2/3 and in the silvex Suspension Order of March 15, 1979 (44 FR 15897), respectively, the Agency is modifying its range definition and correcting an inadvertent error in its pasture definition.

"Range" is now defined as non-pasture grazing land producing forage from native plant species or introduced species managed as native species. Grazing land which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application or other similar practices applied to it is excluded. Forests, defined as land capable of growing 20 cubic feet of wood per year of desirable species which are not withdrawn for non-timber purposes, are also excluded.

"Pasture" is now defined as land producing forage for animal consumption, harvested by grazing, which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application or other similar practices applied to it. Fencerows enclosing pastures are included as part of the pasture.

The modifications in the definitions do not require any modification of the benefits analysis because that analysis was premised on these definitions.

Treatment is generally directed at acreage with severe infestation which, if left uncontrolled, would reduce forage available for livestock grazing.

A number of chemical and non-chemical alternatives to silvex are available to control the various weeds now treated with silvex. However, none of these alternatives is effective against oaks when applied aerially. Thus, effective substitute treatments for silvex must be applied by ground techniques which are more expensive and less convenient. The availability of alternatives and the very small quality of acreage involved indicate that no significant economic impacts will be felt at either the consumer or market levels if silvex is cancelled for this use. At the user level, some increased control costs and decreased production may be experienced by a small number of users. In some locations, the impact on users may be significant.

(2) *Rice.* Although about 98% of all U.S. rice areas are treated with one or more herbicides, silvex is used on only 2,000 acres annually, or less than 0.1% of all U.S. rice acres. In those areas where silvex is used, it is employed to control various broadleaf, aquatic and sedge weeds. These weeds, if not controlled, reduce yield and lower the quality of the rice by contaminating the harvested grain with weed seeds.

There are several chemical alternatives which are likely to be employed as substitutes for silvex use on rice. These compounds may be somewhat less effective and/or more expensive than silvex for use on some weeds. Therefore, some degree of increased control costs and reduced production may be experienced on some acres as a result of the substitution of these materials for silvex. However, because silvex is used on so little rice-growing acreage, the economic impact at the user, consumer and market levels will be quite small if silvex were cancelled for this use.

(3) *Orchard.* Silvex is used on apples and prunes to control preharvest fruit drop and on pears to increase fruit set. Premature drops cause a complete economic loss of prunes and a substantial loss of apple crops. Approximately 50,000 acres of apples (10% of U.S. crop) are treated annually with about 2,500 pounds of silvex. Most of the treated apples are Red Delicious, grown in Washington and several other states, which are sold for fresh consumption. About 8,300 acres of Italian prunes (9% of U.S. acres) grown in Oregon, Washington, and Idaho are treated with about 400 pounds of silvex annually. Treated prunes are believed to be sold primarily for fresh consumption. The extent of silvex usage on pears is unknown.

NAA (1-napthaleneacetic acid) and Alar (succinic acid 2,2-dimethyl hydrazine) probably would be used by apple growers as chemical alternatives to silvex. Some acres would require two annual treatments with these materials for effective control, whereas use of silvex requires only one treatment. The economic impact is likely to consist of higher costs to apple growers, totaling approximately $1 million per year or $20 per average affected acre, resulting from the use of these alternatives. The higher drop control costs will increase production costs by 2–3% per year. Apple production and quality should not be significantly affected.

Prune growers currently using silvex would suffer significant income reductions if silvex is unavailable. Italian and early Italian prunes in the Northwest states drop an average of 35% of the fruit if silvex is not applied in mid-June to control summer drop. Since there are no registered alternatives to silvex for this use, production and revenues would decline sharply on the affected acres. Revenue reductions totaling $1.8 million annually, or about $222 per affected acre, are projected to occur, assuming no alternatives to silvex are developed to prevent preharvest drop. Continued losses of this magnitude would eventually cause growers to grow alternative crops on the estimated 8,300 acres of prunes for which preharvest drop problems are significant.

The retail price of apples and pears would probably be unaffected by cancellation of silvex for orchard use. The retail price of prunes would increase by an undetermined amount.

(4) *Sugarcane.* Silvex is used on sugarcane fields to control weeds not controlled by 2,4-D. Failure to control these weeds can result in reduced yields. About 15% (115,000 acres) of all U.S. sugarcane acres (752,000 acres) were treated with silvex in 1978. This reflects a significant decrease in silvex use over previous years, probably resulting from increased use of an alternative dicamba/2,4-D mixture. The dicamba/2,4-D combination alternative is likely to be the most commonly used substitute if silvex is canceled for use on sugarcane. Economic impacts arising from a cancellation of silvex would result from reduced yield, which would occur because the alternative is less effective than silvex. A worst-case estimate indicates a 2% loss of overall U.S. sugarcane production could be experienced. Since U.S.-produced cane sugar comprises only 18% of the total U.S. sugar supply, no measurable sugar price changes are likely to occur at either the market or consumer levels.

(5) *Non-Crop Uses.*[7] Silvex is registered for control of many broadleaved and herbaceous weeds in a variety of urban and rural non-crop areas such as fencerows, storage areas and parking lots. Only a very small percentage of non-crop areas is treated with silvex each year.

Both chemical and non-chemical controls are available as alternatives to silvex for use on non-crop areas. The chemical alternatives include 2,4-D, pichloram, dicamba, AMS, amitrole. Non-chemical controls include mechanical methods. The relative efficacy of the alternatives in comparison to silvex is unknown. However, it is believed that one or a combination of the chemical alternatives will be widely substituted for silvex and will provide equivalent control.

The economic impact of cancelling silvex for non-crop uses is not likely to be significant at user, consumer or market levels because little acreage is treated with silvex and effective alternatives are readily available.

C. Determinations on Apparent Unreasonable Adverse Effects

For the reasons set forth in detail in PD 1/2/3, the Agency has made the following determinations relating to the apparent unreasonable adverse effects on the nonsuspended uses of silvex:

(1) *Determinations on Rangeland Use.* The Agency has determined that the use of silvex on rangeland appears to pose risks which are greater than the social, economic, and environmental benefits of the use. The Agency has further determined that the available data on the exposure potential and benefits of use on rangeland are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of silvex on rangeland appears generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(2) *Determinations on Rice Use.* The Agency has determined that the use of silvex on rice appears to pose risks which are greater than the social, economic and environmental benefits of

[7] "Non-crop areas" includes: fencerows, hedgerows, fences (not otherwise included among previously suspended uses, e.g. rights-of-way, pasture); industrial sites or buildings (not otherwise included among previously suspended uses, e.g. rights-of-way, commercial/ornamental turf); storage areas, waste areas, vacant and parking lots.

the use. The Agency has further determined that the available data on the exposure potential and benefits of the rice use are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of silvex on rice appears generally to cause unreassonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(3) *Determinations on Sugarcane Use.* The Agency has determined that the use of silvex on sugarcane appears to pose risks which are greater than the social, economic, and environmental benefits of the use. The Agency has further determined that the available data on the exposure potential and benefits of use on sugarcane are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of silvex on sugarcane appears generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(4) *Determinations on Orchard Use.* The Agency has determined that the use of silvex on orchards appears to pose risks which are greater than the social, economic and environmental benefits of the use. The Agency has further determined that the available data on the exposure potential and benefits of the orchard use are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the use of silvex on orchards appears generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

(5) *Determinations on Non-Crop Uses.* The Agency has determined that the use of silvex on fences, lumber yards, refineries, non-food crop areas, storage areas, wastelands, vacant lots, tank farms, industrial sites and other non-crop areas not subject to the emergency suspension orders (i.e., all other non-crop areas except forests, rights-of-way, pastures, home and garden, aquatic weed control/ditch bank and commerical/ornamental turf) appears to pose risks which are greater than the social, economic and environmental benefits of the use. The Agency has further determined that the available data on the exposure potential and benefits of the non-crop uses are to some extent uncertain and/or incomplete, and that the necessary information may be developed through a public hearing for the review of these questions. Accordingly, the Agency has determined that the non-crop uses of silvex appear generally to cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice.

D. Announcement of Regulatory Actions

Based on the determinations summarized above, developed in detail in PD 1/2/3 and PD 4, the Agency is announcing the following regulatory actions, and this document shall constitute its initiation of these actions:

(1) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the use of silvex on rangeland;

(2) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the use of silvex on rice;

(3) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the use of silvex on sugarcane;

(4) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the orchard uses of silvex;

(5) Issuance of a notice of intent to hold a hearing pursuant to FIFRA section 6(b)(2) to determine whether or not to cancel the non-crop uses of silvex.

IV. Statement of Issues

In accordance with § 164.23 of the Agency's Rules of Practice (40 CFR Part 164), this part of the notice states the questions on which evidence relative to the non-suspended uses of silvex shall be taken at the FIFRA section 6(b)(2) hearing.

With respect to the rice, rangeland, and non-crop uses of silvex, evidence will be taken as to the following questions:

(1) Whether the use of silvex on rangeland generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(2) Whether the use of silvex on rice generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(3) Whether the use of silvex on sugarcane generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(4) Whether the use of silvex on orchards generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(5) Whether the use of silvex on non-crop areas generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice;

(6) Whether the use of silvex on rangeland, rice, orchards, and non-crop areas will generally cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice unless the terms and conditions of registration are modified to be more restrictive than those currently in effect; and

(7) Whether, if modifications to the terms and conditions of registration are adopted, the labeling of silvex products for these uses will comply with applicable provisons of FIFRA.

(8) Whether, despite modifications of the terms and conditions of registration, the use of silvex on rangeland, rice, sugarcane, orchards, and non-crop areas will generally cause unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice and should thus be cancelled.

V. Procedural Matters

A. Procedure for Participating in the 6(b)(2) Hearing

Hearings concerning notices issued under section 6(b)(2) of FIFRA are initiated solely at the discretion of the Agency and concern all registrations and uses identified in the statement of issues in the notice.[6] Interested persons may participate in hearings convened by the Agency under FIFRA section 6(b)(2) by filing a timely response in accordance with 40 CFR 164.24.

Section 6(b) of FIFRA provides that any "decision pertaining to registration or classification" of a pesticide which is issued after completion of a section

[6] In contrast, hearings concerning notices of regulatory action issued under section 6(b)(1) of FIFRA are held only if a registrant or other adversely affected party files a valid and timely hearing request and concern only those registrations and uses which are identified in such hearing requests.

6(b)(2) hearing "shall be final." Thus, all registrants and other adversely affected parties who might be affected by cancellation or reclassification of the non-suspended uses of silvex should be aware that participation in the hearing initiated by this notice may constitute their *sole* opportunity to present evidence and/or testimony concerning related issues prior to *final* Agency action. Moreover, judicial review under FIFRA section 16(b) of any action concerning the non-suspended uses of silvex which is taken by the Administrator at the conclusion of the section 6(b)(2) hearing can only be obtained by a person who has been "a party to the proceeding * * *" [9]

All persons who request participation in the hearing initiated by this notice must follow the Agency's Rules of Practice Governing Hearings, 40 CFR Part 164. Section 164.24 of the Rules of Practice provides that each person who wishes to participate in the hearing initiated by this notice must file a written response which satisfies the following requirements:

(1) the response must state the person's position and interest concerning the issues identified in Section IV of this notice; (2) if the person is a registrant or an applicant for registration, the response must specifically identify the registration or application number of each affected pesticide product and include a copy of the currently accepted and/or proposed labeling and a list of the currently registered or proposed uses for each affected pesticide product; and (3) the response must be *received* by the Hearing Clerk within thirty (30) days of publication of this notice in the **Federal Register**. Failure to comply with these requirements will automatically result in denial of the request to participate in the hearing initiated by this notice.

Requests for hearings must be submitted to: Hearing Clerk (A-110), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, D.C. 20460.

[9] It is anticipated that the section 6(b)(2) hearing initiated by this notice will be consolidated with the section 6(b)(1) cancellation hearing concerning the suspended uses of 2,4,5-T and silvex. Thus, it is possible that any person who is already a party in the 6(b)(1) proceeding may be able to obtain judicial review of final Agency action concerning the non-suspended uses of silvex without filing a separate request to participate in the 6(b)(2) proceeding. However, since consolidation of the proceedings is a matter within the sole discretion of the Administrative Law Judge, the Agency recommends that any party who might desire to seek review of any final Agency action concerning currently permissible uses of silvex should file a timely response under 40 CFR § 164.24.

B. Ex Parte Communications

The Agency's Rules of Practice for hearings conducted pursuant to section 6 of FIFRA forbid the Administrator, the Judicial Officer, and the Administrative Law Judge, at all stages of the proceedings, from discussing the merits of the proceedings *ex parte* with any party or with any person who has been connected with the preparation or presentation of the proceeding as an advocate or in an investigative or expert capacity, or with any of their representatives. 40 CFR § 164.7.

Accordingly, the following Agency offices, and the staffs thereof, are designated to perform all investigative and prosecutorial functions in this case: the Office of the Deputy Administrator, the Office of Pesticides and Toxic Substances, the Office of Pesticide Programs, the Office of General Counsel, and the Office of Enforcement.

From the date of this notice until any final decision, neither the Administrative Law Judge, the Judicial Officer, nor the Administrator shall have any *ex parte* contact or communication with any investigative or trial staff employee, or any other interested persons not employed by EPA, on any of the issues involved in this proceeding. However, persons interested in this proceeding should feel free to contact any other EPA employee, including both investigative and trial staff, with any questions they may have.

Dated: December 3, 1979.

Steven D. Jellinek,

Assistant Administrator for Pesticides and Toxic Substances.

2,4,5-T/Silvex Position Document 4—U.S. Environmental Protection Agency, Section Head: Kyle Barbehenn

Position Document 4 for Certain Uses of 2,4,5-Trichlorophenoxyacetic Acid (2,4,5-T) and 2-(2,4,5-Trichlorophenoxy) Propionic Acid (Silvex)

This document represents the conclusion of the Rebuttable Presumption Against Registration (RPAR) process for 2,4,5-T and silvex, and contains the Agency's final determination on regulatory action regarding the uses of 2,4,5-T and silvex which were not suspended on February 28, 1979. In summary, the Agency has reviewed the comments received on its decision, principally those of the FIFRA Scientific Advisory Panel (SAP) and the United States Department of Agriculture (USDA), and now reaffirms its preliminary decision to hold FIFRA 6(b)(2) hearings to determine whether or not to cancel these uses of 2,4,5-T and silvex.

I. Background

On April 11, 1978, the Environmental Protection Agency ("the Agency") issued a notice of rebuttable presumption against registration and continued registration of all pesticide products containing the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) [43 FR 17116, April 21, 1978]. Issuance of the RPAR began the Agency's public review of the registered uses of 2,4,5-T and the uses for which applications for registration are pending. Later, on February 28, 1979, the Administrator ordered the emergency suspension of the use of 2,4,5-T on forests, rights-of-way, and pastures (suspended uses) [44 FR 15874, March 15, 1979].[1] The RPAR review continued for the use of 2,4,5-T on rice, range,[2] and certain non-crop sites (non-suspended uses).

When the suspension orders were issued, silvex was a candidate for RPAR review, but an RPAR notice had *not* been issued. However, the use of silvex on forests, rights-of-way, pastures, homes and gardens, aquatic areas/ditch banks, and commercial/ornamental turf was included in the suspension orders [44 FR 15897, March 15, 1979] because both 2,4,5-T and silvex contain the highly toxic contaminant 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), both have comparable use and correspondingly comparable exposure potential, and both pose risks of adverse effects which are similar in many ways.

The RPAR review of 2,4,5-T and the suspension action prompted the Agency to expedite its RPAR review of the uses of silvex which had not been suspended, namely the use on rangeland, rice, sugarcane, orchards, and non-crop areas[3] (non-suspended uses). As a result of this expedited review, the Agency determined that the non-suspended uses of silvex exceed both the oncogenic and other chronic or delayed toxic effects risk criteria for issuance of an RPAR [40 CFR 162.11(a)(3)].

On July 9, 1979, the Agency issued preliminary notices of determination relating to the non-suspended uses of 2,4,5-T and silvex [44 FR 41531; 44 FR 41536, July 17, 1979]. The Agency

[1] Data and analyses developed in connection with the RPAR review led the Administrator to issue the emergency suspension orders and related notices of intent to cancel the suspended uses of 2,4,5-T and silvex. Suspension hearings began on April 19, 1979, but were discontinued on May 15, 1979, after all registrants withdrew from the hearings and petitioned the Administrator for an expedited cancellation hearing. The formal evidentiary phase of the cancellation hearing is scheduled to begin on January 22, 1980.

[2] See Appendix A, for a clarification of the definition of pasture (suspended use) and rangeland (non-suspended use).

[3] See Table 1.

considered risk information concerning the non-suspended uses of 2,4,5-T and silvex and found (1) that 2,4,5-T and silvex are fetotoxic and teratogenic and (2) that 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), the trace contaminant in 2,4,5-T and silvex, is fetotoxic, teratogenic and carcinogenic. The Agency acknowledged that there are some uncertainties about the amount of human exposure to 2,4,5-T, silvex, and TCDD because of the limited exposure information available.

Table 1.—*Suspended and Nonsuspended Uses of 2,4,5-T and Silvex*

	2,4,5-T	Silvex
Nonsuspended uses: [2,4,5-T RPAR issued April 21, 1978 (43 FR 17116); silvex RPAR issued July 17, 1979 (44 FR 41536)].	Rice, range, noncrop sites[1].	Rice, range, noncrop sites,[1] sugarcane, orchards.
Suspended uses: [2,4,5-T emergency suspension issued March 15, 1979 (44 FR 15674); silvex emergency suspension issued March 15, 1979 (44 FR 15697)].	Forests, rights-of-way, pasture.	Forests, rights-of-way, pasture, home and garden, aquatic areas/ditch banks, commercial/ornamental turf.

[1] Includes use on or around noncrop sites, such as fencerows, hedgerows, fences (not otherwise included in suspended uses; e.g., rights-of-way, pasture); industrial sites or buildings (not otherwise included in suspended uses; e.g., rights-of-way, commercial/ornamental turf); storage areas, waste areas, vacant lots, parking areas, and all other noncrop sites.

Concerning the non-suspended uses of 2,4,5-T and silvex, the Agency has also considered economic benefits information which pesticide registrants, the United States Department of Agriculture, and other interested parties originally submitted in response to the 2,4,5-T RPAR notice. During the course of the review, the Agency weighed risks and benefits to determine whether or not the risks of each use were exceeded by the corresponding benefits. The Agency determined that additional benefits data were being developed which merit consideration, especially for the non-suspended uses of silvex.

Accordingly, with respect to the non-suspended uses of 2,4,5-T and silvex, the Agency has concluded: (1) that continued use of these two chemicals appears to cause unreasonable adverse effects on the environment, (2) that there are uncertainties in the data relating to the risks and benefits of the uses at issue, (3) that additional data on the risks and benefits of the non-suspended uses of 2,4,5-T and silvex will permit the Agency to determine whether or not to cancel the registrations for these uses, and (4) that such information can be acquired through a public hearing under section 6(b)(2) of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, 7 U.S.C. Section 136 *et seq.* (FIFRA).

Under FIFRA, the Agency is required to submit these preliminary *determinations to the Scientific* Advisory Panel for comment on risk issues, and to the United States Department of Agriculture for comment on benefits issues. The Agency must then respond publicly to the comments made by the SAP and the USDA before making a final regulatory decision (7 U.S.C. 136d). The remainder of this document sets forth the Agency's analysis of comments submitted by USDA, the SAP, and other interested parties, and the Agency's reasons and the factual base for the action it is taking. The formal comments submitted by the SAP and the USDA are reproduced in their entirety as Appendices B and C of this document.

II. Issues Relating to Risk

A. Comments Relating to Toxicity

The Agency's proposed action is based in part on data that show 2,4,5-T, silvex, and/or TCDD produce fetotoxic, teratogenic, and carcinogenic effects in test animals. The SAP agreed with the Agency's assessment of the toxic effects of these chemicals but did not fully agree on all aspects of its interpretation of dose level responses.

(1) *Reproductive Toxicity.* In previous position and suspension documents, the Agency cited numerous studies in test species which showed that 2,4,5-T or silvex containing 0.5 parts per million (ppm) or less TCDD and pesticide-free TCDD produce cleft palate, kidney abnormalities, delayed ossification, fetal mortality, and reduced fetal weight (see 43 FR 17116, April 21, 1978 and 44 FR 15674, March 15, 1979 for review). In rodents, adverse effects were noted at maternal doses as low as 10 milligrams per kilogram (mg/kg) body weight 2,4,5-T (0.05 ppb TCDD) [Smith, 1978]; 50 mg/kg silvex body weight (<0.05 ppm TCDD) [Dow, 1973]; and 0.001 micrograms per kilogram (ug/kg) body weight TCDD (Murray, 1979; Smith et al., 1976). Furthermore, in non-human primates, maternal doses of TCDD as low as 50 parts per trillion (ppt) [about 0.002 ug/kg] resulted in reduced fertility and increased fetal loss (Schantz et al., 1979). Similar and more severe effects have been observed at higher doses in all species tested. Because statistically significant effects consistent with those seen at higher doses were observed at 0.001 ug/kg TCDD in a three generation study in rats, and because this is the lowest dose tested in any species, the Agency has determined that a no-observed effect level (NOEL) has not been demonstrated for fetotoxic effects due to TCDD exposure.

The SAP agreed with the Agency that 2,4,5-T, silvex, and TCDD are each teratogenic and fetotoxic. The SAP also agreed that a NOEL had not been established for TCDD in monkeys. However, the SAP concluded that "for all practical purposes" a NOEL has been shown for TCDD in studies with rats and mice. Although the SAP concluded that 0.001 ug/kg was a practical NOEL, the Panel also recognized the existence of effects at this dose level. While the Agency interpreted these effects as significant, and sufficient to preclude establishment of a NOEL, the Panel interpreted them as suggestive of a NOEL.

Without additional data, the Agency is reluctant to adopt the Panel's interpretation. TCDD is one of the most toxic chemicals known. Its degree of toxicity, as well as its toxic manifestations, varies among the animal species, and its effects on the human reproductive system are largely unknown. In addition, the control data upon which the study is based are so variable as to warrant concern that these fluctuations may be masking additional effects. Because the effects seen at 0.001 ug/kg are consistent with those seen at higher doses, and because of the factors listed above, the Agency is unwilling to dismiss the effects observed at 0.001 ug/kg as insignificant to risk assessment. Extrapolations from experimental animal studies to man are difficult even when there is a clear NOEL. When, with TCDD, there is no NOEL, the Agency would prefer to err on the side of safety.

(2) *Oncogenicity.* In Position Document 2/3 on 2,4,5-T and Position Document 1/2/3 on silvex, the Agency concluded that commercial 2,4,5-T and silvex may pose a significant carcinogenic risk to exposed humans. This conclusion was based primarily on data showing that TCDD, an unavoidable contaminant in commercial

2,4,5-T and silvex, is carcinogenic in laboratory animals.

The principal comments made by the SAP regarding the oncogenicity of 2,4,5-T, silvex, and TCDD, together with the Agency's response to these comments, are summarized below.

The SAP agreed with the Agency that TCDD is carcinogenic in laboratory animals. The SAP also agreed that commercial 2,4,5-T products pose some oncogenic risk to man because of contamination of these products with TCDD. However, the SAP concluded that the available evidence indicates that there is no substantial oncogenic risk to man from exposure to commercial 2,4,5-T.

The Agency disagrees with this conclusion. When the SAP considered the Agency's proposed Section 6(b)(2) notices for 2,4,5-T and silvex, the Agency had not yet completed its exposure analysis. The exposure information provided to the SAP was thus not a sufficient basis for making an accurate determination on whether or not the oncogenic risk posed by the uses of 2,4,5-T affected by the proposed notices was substantial. An accurate determination may be possible when the Agency completes its exposure analysis.

The SAP stated that the CAG concluded that the non-oncogenic dose [in the study by Kociba et al. (1978) on TCDD] lies between 0.01 and 0.001 mg/kg/day. The Agency, however, contends that the CAG concluded only that no oncogenic response was *observed* in the Kociba study at a dose of 0.001 mg/kg/day. On the basis of the no-threshold dose response theory regarding carcinogenicity (Albert et al., 1977), the CAG and the Agency consider any dose of TCDD, no matter how small, to pose some carcinogenic risk to humans.

The SAP concluded that the few oncogenicity studies on silvex which have been conducted do not indicate any oncogenic effects, but commented nonetheless that "these data must be viewed with some caution because of the contamination of commercial silvex with TCDD."

The Agency agrees with the SAP that any chronic studies on silvex which have not demonstrated a carcinogenic response should be viewed with caution. Because TCDD is an unavoidable contaminant of commercial silvex, the Agency concludes that silvex poses some carcinogenic risk to exposed humans. A determination of the substantiability of this risk may be possible when the Agency completes its exposure analysis.

Certain other comments by the SAP reflect differences of opinion among scientists concerning other technical details which have no direct bearing on the Agency's proposal to hold a 6(b)(2) hearing. Such a hearing provides an appropriate forum for an in-depth development and analysis of the issues and the Agency thus feels that it is not necessary to respond to several of the SAP's comments on oncogenicity at this time.

B. Comments Relating to Exposure and Risks

On the question of potential human exposure to 2,4,5-T, silvex, and/or TCDD from the non-suspended uses, the Agency and the SAP are in agreement on the need for additional data. In reaching a preliminary decision, the Agency concluded that although the non-suspended uses appear to cause unreasonable risks of adverse effects, at present, gaps in the data preclude an accurate assessment of the potential for human hazards. In particular, the Agency specified a need for additional information on possible avenues of human exposure. The SAP also concluded that there is a potential for human exposure from the non-suspended uses, but that the available data are "incomplete and preliminary in nature". The SAP specifically recommended that additional monitoring data be obtained from sources likely to demonstrate human exposure, placing particular emphasis on TCDD levels.

(1) *Monitoring Data.* In the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, the Agency presented data from STORET, a computerized data base of surface water chemical residues, and from the National Surface Water Monitoring Program for Pesticides (NSWMPP), which indicate that 2,4,5-T and silvex residues were present in water in areas where these herbicides are used. The Agency acknowledged that these residues could not be attributed to specific uses of 2,4,5-T and silvex. However, the Agency's concern about these residues in the environment was supported by monitoring studies in rangeland (Marigold and Schulze, 1969; Lawson, 1976) and apple orchard areas (Cochran et al., 1976).

Concern about potential human exposure to 2,4,5-T, silvex, and/or TCDD from the non-suspended uses has prompted the Agency to undertake new monitoring studies. As indicated in the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, rice, crayfish, catfish, water, and sediment from the South are being tested to determine the extent of environmental contamination due to 2,4,5-T and silvex use on rice. The Agency is also engaged in monitoring edible fish, rice, sediment, human milk, beef fat, and beef liver for TCDD residues.

During the SAP meeting of August 15, 1979, the Agency acknowledged that there is not a large body of monitoring data available for specific uses because previously reported monitoring projects were rarely use-oriented and were frequently conducted at times when the chemical was not being used in the monitored area. Therefore, residues traceable to a particular chemical use might not be detected under these circumstances.

The SAP concurred with the Agency's view that available monitoring data are inadequate to assess potential human exposure from the uses of 2,4,5-T on rice, range, and certain non-crop sites, and from the use of silvex on orchards, rice, range, sugarcane, and certain non-crop sites. The SAP characterized the monitoring data presented by the Agency as incomplete and preliminary in nature and recommended that additional data be gathered regarding the levels of 2,4,5-T, silvex, and TCDD in milk, tissues of range animals, and edible aquatic organisms.

As indicated above, the Agency is currently conducting several significant monitoring studies in the media recommended by the SAP. In addition, the Agency is reviewing recent monitoring studies by other researchers, such as another TCDD study in human milk (Memo, 1979c) and a TCDD study in fish (Kuehl et al., 1979). The results of these studies will be reviewed during the 6(b)(2) hearings.

(2) *Risk Comments.* The SAP made several comments on the issues of exposure and risk, and on the methods of risk reduction with which the Agency disagrees. The Panel concluded that the margins of safety between exposure and the NOEL were sufficient to protect the general population from any reproductive risk associated with the non-suspended uses of 2,4,5-T and silvex. Concerning mixers and loaders, the SAP suggested that risk could be reduced to a safe level by the use of protective clothing and equipment. The Agency's disagreement with the Panel's adoption of a "for all practical purposes" NOEL for TCDD has been discussed above. The Agency further questions whether the existing data are sufficient to permit the Panel's conclusion that protective clothing and equipment are sufficient to adequately reduce risk for mixers and loaders.

In addition, the SAP recommended that efforts be made to reduce the TCDD content in commercial 2,4,5-T and silvex. Although the Agency applauds any efforts by registrants to reduce

TCDD levels in pesticide products containing 2,4,5-T and silvex, any review of these chemicals at this time can be based only on the present formulations of 2,4,5-T and silvex products which unavoidably contain TCDD. As for all other pesticides, 2,4,5-T and silvex registrants must provide the Agency with scientific data, through the registration process, that the production of 2,4,5-T and/or silvex without TCDD does not cause unreasonable adverse effects to human health or the environment.

C. Comment Relating to New Data

In addition to its comments on the Agency's assessment of existing data, the Panel urged the Agency to review new data from several on-going and recently completed studies. Specifically, the SAP recommended that a full set of details be obtained and evaluated concerning new oncogenicity studies conducted by Leuschner et al. (1979) with 2,4,5-T containing less than 0.05 ppm TCDD and by the National Cancer Institute [NCI] (1979) with TCDD. Also, the SAP recommended similar measures for Dr. James Allen's on-going reproductive toxicity study in monkeys fed a diet containing 25 ppt TCDD (Allen, 1979).

This recommendation is fully consistent with the Agency's customary practice of evaluating new information as part of its continuing review of risks and benefits of registered chemicals. The Agency will review and assess these and any other available studies in the context of the proposed 6(b)(2) hearings.

In conclusion, the Agency has determined that the SAP comments do not warrant a change in the Agency's risk analysis for the non-suspended uses of 2,4,5-T and silvex at this time.

III. Issues Relating to Benefits

In the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3, the Agency provided a preliminary benefits analysis and acknowledged that further review of the chemical alternatives was necessary before the Agency could make a final assessment of the risks and benefits associated with the continued uses of 2,4,5-T and silvex. Throughout the review of 2,4,5-T and silvex, the Agency has expressed concern about the quality and completeness of much of the data it has obtained on the economic benefits of 2,4,5-T and silvex.

In its response to the Agency's proposal, USDA agreed that these data gaps can best be addressed through a 6(b)(2) hearing for the non-suspended uses of 2,4,5-T and silvex. USDA did not provide substantive comment on the benefits determinations which were presented in the Position Documents. In addition, USDA stated its intention to continue assembling additional data to be submitted to the Agency on the uses of, and benefits associated with, these herbicides. The Agency is also continuing to gather benefits information from other sources.

In conclusion, the USDA's comments on the Agency's preliminary benefits analysis for the non-suspended uses of 2,4,5-T and silvex wholly support the Agency's determination that further review is necessary and can best be addressed through a 6(b)(2) hearing.

IV. Conclusion

The SAP's assessment of the scientific data on the reproductive and the oncogenic effects of 2,4,5-T, silvex, TCDD in test animals is generally consistent with the Agency's position. Also, consistent with the Agency's current efforts were several SAP recommendations for obtaining additional data.

The Panel concluded that it had found no evidence of an "immediate or substantial hazard" to human health or the environment associated with the non-suspended uses, and is likewise the Agency's position. Upon finding evidence of an "imminent hazard", the Agency acts to suspend the pesticide uses which are implicated. An example of such action is the recent emergency action suspending certain uses of 2,4,5-T and silvex.

As was discussed in the 2,4,5-T Position Document 2/3 and the Silvex Position Document 1/2/3 for the non-suspended uses, the Agency recommends holding a hearing, in part because the available data indicates that these uses appear to have unreasonable adverse effects on the environment. However, the Agency did not act to suspend these uses as it would have done if it had found an imminent hazard.

The SAP disagreed with the Agency's proposal to hold a hearing and recommended that the Agency not hold a 6(b)(2) hearing at this time. The Agency has taken the Panel's recommendations into account but has decided that such a hearing is appropriate, based on (1) information showing that the non-suspended uses of 2,4,5-T and silvex appear to cause unreasonable adverse effects on man or the environment, (2) the Agency's and the SAP's conclusion that more information is necessary to resolve the issues involved, and (3) that a combined hearing is the most efficient and effective way to resolve the issues.

The Agency holds that it is in the public interest to combine the hearing for the nonsuspended uses with the cancellation hearing for those uses that were suspended on February 28, 1979. Not only will this action be administratively convenient for the Agency, registrants, and interested parties, entailing more efficient use of resources, but it will also ensure that the Agency's concerns on all uses of 2,4,5-T and silvex are addressed consistently.

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Appendix A

In response to comments expressing confusion about the Agency's pasture and range definitions, the Agency is taking this opportunity to correct an inadvertant error in the pasture definition and to modify the range definition.

In the pasture definition the word "and" was inserted in the list of cultural practices in place of the intended word "or" (44 FR 15874; 44 FR 15897, March 15, 1979). Therefore, the definition should be corrected by the substituting of the word "or" for "and" so that the definition now reads as follows:

Pasture is defined as land producing forage for animal consumption, harvested by grazing, which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application or other similar practices applied to it. Fencerows enclosing pastures are included as part of the pasture.

This correction clearly specifies that annual application of any one or more of these cultural practices will classify the land as pasture.

The following modification of the range definition will further explain the distinction between range and pasture. These modifications are based on the same USDA Forest Service material which was the source for EPA's definition of pasture and range. With these modifications, range is now defined as follows:

Range is non-pasture grazing land producing forage from native plant species or introduced species managed as native species. Grazing land which has annual or more frequent cultivation, seeding, fertilization, irrigation, pesticide application, or other similar practices applied to it is excluded. However, forests [1], as defined in 44 FR 15893, March 15, 1979, are excluded.

[1] Lands capable of growing 20 cubic feet of wood per acre per year of desirable species which are not withdrawn for non-timber purposes.

Appendix B.—Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Scientific Advisory Panel

Review of Notices of Intent To Hold FIFRA Section 6(b)(2) Hearing on 2,4,5-T and Silvex

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel has completed review of the Notices of Intent by the Environmental Protection Agency (EPA) to hold hearings under the provisions of FIFRA section 6(b)(2) to consider appropriate regulatory action for those uses of 2,4,5-T and Silvex which were not included in the recent suspension orders. The review was completed in open meetings held in Arlington, Virginia, during the periods August 15-16, 1979, and September 20, 1979.

Maximum public participation was encouraged by the Scientific Advisory Panel to ensure an objective and adequate consideration of all relevant scientific issues relating to health and the environment. Public notice of the meetings was published in the Federal Register on July 27, 1979, and September 4, 1979. In addition, telephonic calls and special mailings were also sent to the general public who had previously expressed an interest in activities of the Panel.

Written statements relative to 2,4,5-T and Silvex were received from Dow Chemical Company, and Michigan State University.

In addition, oral comments were received from Dr. J. R. Allen, University of Wisconsin Medical School; EPA technical staff; representatives of the Texas State Department of Agriculture; Dow Chemical Company; and the Environmental Defense Fund.

The FIFRA Scientific Advisory Panel wishes to recognize the excellent cooperation and assistance of numerous EPA technical staff throughout the review of 2,4,5-T and Silvex.

In consideration of all matters brought out during the meeting and careful review of all documents submitted by the Agency and other parties, the Panel unanimously submits the following report:

In response to the Agency's request for advice concerning whether a FIFRA section 6(b)(2) hearing should be held to resolve questions relative to the continued use of 2,4,5-T and Silvex on rice, rangeland, orchards, sugarcane, and certain non-crop sites, (1) *the Scientific Advisory Panel recommends that the Agency not hold such a meeting at this time.* After extensive review of the data we find no evidence of an immediate or substantial hazard to human health or to the environment associated with the use of 2,4,5-T or Silvex on rice, rangeland, orchards, sugarcane, and the non-crop uses specified in the decision documents.

The Scientific Advisory Panel has extensively reviewed the animal toxicity test data base for teratogenesis, carcinogenesis, and reproductive effects for 2,4,5-T, Silvex, and TCDD and has identified some additional data needs which should be addressed prior to final decision making relative to the safety evaluation of 2,4,5-T and Silvex. (2) *The Scientific Advisory Panel recommends specifically that the full details be obtained and evaluated for the following three studies which were discussed briefly at the hearing:*

1. The oncogenicity study on commercial 2,4,5-T being conducted in Germany in the Laboratorium Fur Pharmakologie Und Toxikologie. An oncogenic study has recently been completed on 2,4,5-T which was specially purified to contain a low concentration of TCDD. However, data is needed on the oncogenicity of commercial 2,4,5-T containing TCDD (≥ 0.05 ppm).

2. The oncogenicity study recently completed at NCI with TCDD in both rats and mice; and

3. The reproductive toxicity study being conducted at the University of Wisconsin by Dr. Allen in which monkeys are being fed a diet containing TCDD at 25 ppt.

The Scientific Advisory Panel has also reviewed the available data regarding potential human exposure to 2,4,5-T and Silvex from use on rice, rangeland, orchards, sugarcane, and other non-crop applications and the monitoring data related to these uses and would characterize these as incomplete and preliminary in nature. (3) *We therefore recommend that monitoring data be obtained regarding the levels of 2,4,5-T and Silvex and TCDD in milk, and that additional data be gathered regarding the levels of these agents in the tissues of range animals and that information be obtained regarding the levels of these agents in edible aquatic organisms.* In these additional monitoring studies special emphasis should be placed on TCDD levels rather than levels of 2,4,5-T and Silvex, *per se.*

In regard to the specific issues and questions posed by the Agency to the Panel regarding review of 2,4,5-T and Silvex, the Scientific Advisory Panel offers the following responses:

Issues on Toxicology

Question 1. EPA has found that 2,4,5-T, Silvex, and TCDD are teratogens. Does the Panel agree?

Response: The Scientific Advisory Panel agrees with the Agency that 2,4,5-T, Silvex, and TCDD are teratogens.

Question 2. EPA has found that 2,4,5-T, Silvex, and/or TCDD are fetotoxins. Does the Scientific Advisory Panel agree?

Response: The Scientific Advisory Panel agrees with the Agency that 2,4,5-T, Silvex, and TCDD produce reproductive (fetotoxic) effects.

Question 3. EPA has determined that TCDD exhibits fetotoxic effects and that a No Observable Effect Level (NOEL) has not been established for this effect. Does the Scientific Advisory Panel agree with this finding?

Response: The Panel agrees with the Agency that a NOEL has not been established for TCDD in chronic studies in monkeys. In contrast to the Agency position, the Panel concludes that a NOEL has been established for TCDD for both rats and mice. The Scientific Advisory Panel would like to point out in this regard that the Agency position is relatively close to that of the scientists from the Dow Chemical Company. The Scientific Advisory Panel believes that the dose of 0.001 ug/kg/day is for all practical purposes a NOEL (For the purposes of risk calculation; See Appendix I). It should be

pointed out that a NOEL for reproductive effects has been established for commercial 2,4,5-T in all species tested including monkeys.

Question 4. EPA has found that TCDD is carcinogenic in test animals, and thus is a potential human carcinogen. Does the Scientific Advisory Panel concur with this finding?

Response: The Scientific Advisory Panel agrees with the Agency opinion that TCDD is carcinogenic in test animals and therefore may be a potential human carcinogen.

Question 5. EPA has found that TCDD is an extremely potent animal carcinogen. Does the Scientific Advisory Panel agree with this finding?

Response: Answered in question 4 above.

Issues on Exposure

Question 1. EPA believes that human exposure from the use of 2,4,5-T and Silvex on rice may be broad and substantial due to herbicide drift during and after application, and that more diffuse exposure is possible through the water environment and through crayfish, catfish and other food sources. How would the Panel characterize the exposure potentials and concerns for rice use? What questions do they have and how would they be answered by the proposed monitoring plan?

Response: The Scientific Advisory Panel agrees that exposure to 2,4,5-T and Silvex from use on rice may be possible through the water environment and through edible aquatic organisms and other food sources. However, the Scientific Advisory Panel believes that insufficient data was presented or made available to the Panel in support of the argument that human exposure from spray drift and the water environment is likely to be broad or substantial. The questions regarding proposed monitoring have already been addressed. In addition to the need for more data on the concentrations of Silvex, 2,4,5-T, and TCDD in crayfish and catfish, monitoring data should also be obtained on soil sediments.

Question 2. EPA believes that drift from the use of 2,4,5-T/Silvex products on rangeland creates a lower, yet-still-real, potential for exposure due to lower population densities and distribution in range areas relative to rice growing areas. Sparsity of surface water and extreme depth of ground water in many areas would suggest a minimal exposure from aquatic sources used as food. However, beef monitoring shows low levels of dioxin in a limited number of samples from beef that grazed on 2,4,5-T treated range. How would the Panel characterize the exposure potential and concerns for the use of these chemicals on range? What unanswered questions do they believe the Agency should address in determining exposure potential?

Response: The Scientific Advisory Panel agrees with the Agency that there is a potential for exposure as a result of drift from the use of 2,4,5-T and Silvex products on rangeland and that the potential for exposure from this mechanism would be lower than that from use of the agents on rice. However, the Panel believes that the data made available to the Panel did not provide a convincing argument for the existence of an immediate or substantial hazard from the use of Silvex and 2,4,5-T on rangelands.

Question 3. Little is known about the potential for dietary exposure to Silvex and/or TCDD from the uses of Silvex on food crops, except for apples on which Silvex residues have been detected. Given the nature of the contaminant TCDD, EPA has reason for presuming that exposure to food consumers and the environment is possible from these uses. What are the Panel's views on the potential for ingestion exposure from these uses?

Response: Although there is information on the use patterns of Silvex in orchard crops, the Scientific Advisory Panel believes sufficient residue data is not currently available for a definitive opinion on dietary exposure to Silvex.

Question 4. The Agency believes that TCDD and 2,4,5-T move in water from rice to other environmental compartments thereby increasing exposure to widely diffuse populations. Does the Scientific Advisory Panel concur with this?

Response: The Panel agrees with the Agency that it would be possible for 2,4,5-T to move in water from rice fields to other environmental compartments and to thereby increase exposure to widely diffuse populations. However, we believe such movement would be unlikely for TCDD.

General Issues

Question 1. Do the residues (2,4,5-T, Silvex and TCDD) in water, sediment, aquatic organisms and/or the potential for exposure from herbicide drift, in light of the toxicological attributes of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No (See recommendation (1).)

Question 2. Can the Scientific Advisory Panel assess whether the residues being found in the rice areas are due to the rice use or to other previously permitted uses?

Response: The Panel is not aware of data sufficient to answer this question (See recommendation (3).)

Question 3. Do the exposure potentials in range use, in light of the toxicological characteristics of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No. (However, see recommendation (3).)

In consideration of the potential toxicity of TCDD, (4) *the Scientific Advisory Panel recommends that efforts should be made to further reduce the level of chemical TCDD in commercial preparations of 2,4,5-T and Silvex.*

Dated: September 26, 1979.

For the Chairman.

Certified as an accurate report of findings.

Wade Fowler, Jr.,

Executive Secretary, FIFRA Scientific Advisory Panel.

Appendix I.—The FIFRA Scientific Advisory Panel Evaluation of the Oncogenicity, Fetotoxity, and Exposure Characteristics for 2,4,5-T, Silvex and TCDD

Introduction

In our opinion the major health and environmental issues relative to possible regulatory action by the Agency center around the potential of commercial forms of 2,4,5-T and Silvex contaminated with TCDD to pose carcinogenic, teratogenic and reproductive risks to persons as a result of (1) exposure during mixing and application, or (2) direct exposure to the spray as a result of living in the immediate area of application. In contrast, the major concern relative to TCDD, essentially free of 2,4,5-T or Silvex, arises from the degree to which this agent concentrates in portions of the human food chain. The primary concern of the Scientific Advisory Panel is the potential carcinogenic, reproductive, and teratogenic risk from use of commercial 2,4,5-T and Silvex contaminated with TCDD. The potential for these same risks from TCDD essentially free of 2,4,5-T and Silvex is of secondary concern, as is the potential risk posed by 2,4,5-T or silvex essentially free of TCDD.

Commercial 2,4,5-T

Oncogenicity. Seven studies of variable quality have been carried out in mice to examine the oncogenicity of commercial 2,4,5-T contaminated with TCDD. The results of these studies have not demonstrated a carcinogenic risk from commercial 2,4,5-T in this rodent species. A complete study of the carcinogenic potential of commercial 2,4,5-T contaminated with TCDD at ≦0.05 ppm has not yet been reported in rats. However, such a study has recently been completed by the Laboratorium for Pharmakologie and Toxikologie, Hamburg, Germany. The Scientific Advisory Panel was informed during the recent meeting that gross autopsy examination of these animals revealed no increase in tumors relative to the control groups. However, until the pathological examination is complete no definitive conclusion can be drawn relative to the oncogenic potential of commercial 2,4,5-T in rats. The Dow Chemical Company has recently completed a study of the oncogenicity of a specially purified sample of 2,4,5-T in rats. This sample of 2,4,5-T contained less than 0.0003 ppm TCDD. In this study there was no increase in tumors resulting from exposure to this purified preparation of 2,4,5-T fed at the maximum tolerated dose (30 mg/kg/day) or at lower doses (10 mg/kg/day and 3 mg/kg/day). Thus it appears that 2,4,5-T, which is essentially free of contaminating TCDD, is not oncogenic in rats. However, this study is of limited predictive value since the form of 2,4,5-T of concern to the Scientific Advisory Panel is commercial 2,4,5-T; in other words, 2,4,5-T contaminated with TCDD.

Chronic tests carried out using TCDD free of 2,4,5-T have demonstrated that TCDD is

pointed out that a NOEL for reproductive effects has been established for commercial 2,4,5-T in all species tested including monkeys.

Question 4. EPA has found that TCDD is carcinogenic in test animals, and thus is a potential human carcinogen. Does the Scientific Advisory Panel concur with this finding?

Response: The Scientific Advisory Panel agrees with the Agency opinion that TCDD is carcinogenic in test animals and therefore may be a potential human carcinogen.

Question 5. EPA has found that TCDD is an extremely potent animal carcinogen. Does the Scientific Advisory Panel agree with this finding?

Response: Answered in question 4 above.

Issues on Exposure

Question 1. EPA believes that human exposure from the use of 2,4,5-T and Silvex on rice may be broad and substantial due to herbicide drift during and after application, and that more diffuse exposure is possible through the water environment and through crayfish, catfish and other food sources. How would the Panel characterize the exposure potentials and concerns for rice use? What questions do they have and how would they be answered by the proposed monitoring plan?

Response: The Scientific Advisory Panel agrees that exposure to 2,4,5-T and Silvex from use on rice may be possible through the water environment and through edible aquatic organisms and other food sources. However, the Scientific Advisory Panel believes that insufficient data was presented or made available to the Panel in support of the argument that human exposure from spray drift and the water environment is likely to be broad or substantial. The questions regarding proposed monitoring have already been addressed. In addition to the need for more data on the concentrations of Silvex, 2,4,5-T, and TCDD in crayfish and catfish, monitoring data should also be obtained on soil sediments.

Question 2. EPA believes that drift from the use of 2,4,5-T/Silvex products on rangeland creates a lower, yet still-real, potential for exposure due to lower population densities and distribution in range areas relative to rice growing areas. Sparsity of surface water and extreme depth of ground water in many areas would suggest a minimal exposure from aquatic sources used as food. However, beef monitoring shows low levels of dioxin in a limited number of samples from beef that grazed on 2,4,5-T treated range. How would the Panel characterize the exposure potential and concerns for the use of these chemicals on range? What unanswered questions do they believe the Agency should address in determining exposure potential?

Response: The Scientific Advisory Panel agrees with the Agency that there is a potential for exposure as a result of drift from the use of 2,4,5-T and Silvex products on rangeland and that the potential for exposure from this mechanism would be lower than that from use of the agents on rice. However, the Panel believes that the data made available to the Panel did not provide a convincing argument for the existence of an immediate or substantial hazard from the use of Silvex and 2,4,5-T on rangelands.

Question 3. Little is known about the potential for dietary exposure to Silvex and/or TCDD from the uses of Silvex on food crops, except for apples on which Silvex residues have been detected. Given the nature of the contaminant TCDD, EPA has reason for presuming that exposure to food consumers and the environment is possible from these uses. What are the Panel's views on the potential for ingestion exposure from these uses?

Response: Although there is information on the use patterns of Silvex in orchard crops, the Scientific Advisory Panel believes sufficient residue data is not currently available for a definitive opinion on dietary exposure to Silvex.

Question 4. The Agency believes that TCDD and 2,4,5-T move in water from rice to other environmental compartments thereby increasing exposure to widely diffuse populations. Does the Scientific Advisory Panel concur with this?

Response: The Panel agrees with the Agency that it would be possible for 2,4,5-T to move in water from rice fields to other environmental compartments and to thereby increase exposure to widely diffuse populations. However, we believe such movement would be unlikely for TCDD.

General Issues

Question 1. Do the residues (2,4,5-T, Silvex and TCDD) in water, sediment, aquatic organisms and/or the potential for exposure from herbicide drift, in light of the toxicological attributes of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No (See recommendation (1).)

Question 2. Can the Scientific Advisory Panel assess whether the residues being found in the rice areas are due to the rice use or to other previously permitted uses?

Response: The Panel is not aware of data sufficient to answer this question (See recommendation (3).)

Question 3. Do the exposure potentials in range use, in light of the toxicological characteristics of these compounds, suggest to the Scientific Advisory Panel the possibility of significant risk?

Response: No. (However, see recommendation (3).)

In consideration of the potential toxicity of TCDD, (4) *the Scientific Advisory Panel recommends that efforts should be made to further reduce the level of chemical TCDD in commercial preparations of 2,4,5-T and Silvex.*

Dated: September 26, 1979.

For the Chairman.

Certified as an accurate report of findings.

Wade Fowler, Jr.,

Executive Secretary, FIFRA Scientific Advisory Panel.

Appendix I.—The FIFRA Scientific Advisory Panel Evaluation of the Oncogenicity, Fetotoxity, and Exposure Characteristics for 2,4,5-T, Silvex and TCDD

Introduction

In our opinion the major health and environmental issues relative to possible regulatory action by the Agency center around the potential of commercial forms of 2,4,5-T and Silvex contaminated with TCDD to pose carcinogenic, teratogenic and reproductive risks to persons as a result of (1) exposure during mixing and application, or (2) direct exposure to the spray as a result of living in the immediate area of application. In contrast, the major concern relative to TCDD, essentially free of 2,4,5-T or Silvex, arises from the degree to which this agent concentrates in portions of the human food chain. The primary concern of the Scientific Advisory Panel is the potential carcinogenic, reproductive, and teratogenic risk from use of commercial 2,4,5-T and Silvex contaminated with TCDD. The potential for these same risks from TCDD essentially free of 2,4,5-T and Silvex is of secondary concern, as is the potential risk posed by 2,4,5-T or silvex essentially free of TCDD.

Commercial 2,4,5-T

Oncogenicity. Seven studies of variable quality have been carried out in mice to examine the oncogenicity of commercial 2,4,5-T contaminated with TCDD. The results of these studies have not demonstrated a carcinogenic risk from commercial 2,4,5-T in this rodent species. A complete study of the carcinogenic potential of commercial 2,4,5-T contaminated with TCDD at ≦0.05 ppm has not yet been reported in rats. However, such a study has recently been completed by the Laboratorium for Pharmakologie and Toxikologie, Hamburg, Germany. The Scientific Advisory Panel was informed during the recent meeting that gross autopsy examination of these animals revealed no increase in tumors relative to the control groups. However, until the pathological examination is complete no definitive conclusion can be drawn relative to the oncogenic potential of commercial 2,4,5-T in rats. The Dow Chemical Company has recently completed a study of the oncogenicity of a specially purified sample of 2,4,5-T in rats. This sample of 2,4,5-T contained less than 0.0003 ppm TCDD. In this study there was no increase in tumors resulting from exposure to this purified preparation of 2,4,5-T fed at the maximum tolerated dose (30 mg/kg/day) or at lower doses (10 mg/kg/day and 3 mg/kg/day). Thus it appears that 2,4,5-T, which is essentially free of contaminating TCDD, is not oncogenic in rats. However, this study is of limited predictive value since the form of 2,4,5-T of concern to the Scientific Advisory Panel is commercial 2,4,5-T; in other words, 2,4,5-T contaminated with TCDD.

Chronic tests carried out using TCDD free of 2,4,5-T have demonstrated that TCDD is

carcinogenic in rats and carcinogenic or tumorigenic in mice. Thus, since commercial 2,4,5-T contains TCDD as a contaminant (≦0.05 ppm) the lack of a carcinogenic response in rodents using commercial 2,4,5-T must be viewed with caution. The Scientific Advisory Panel is of the opinion that some carcinogenic risk to man is posed by exposure to 2,4,5-T contaminated with TCDD at the level present in the 2,4,5-T in current use. However, the data currently available indicate that this risk is not substantial.

In summary, the evidence currently available indicates there is not an immediate or substantial oncogenic risk to man from exposure to 2,4,5-T contaminated with TCDD at a level of ≦0.05 ppm.

Reproductive and Embryo Toxicity

Commercial 2,4,5-T produces fetal toxicity and is teratogenic in rats and mice. According to the data presented to the Scientific Advisory Panel during the August 15-16, 1979 meeting, the no effect level for embryo toxicity for commercial 2,4,5-T in various species when examined in conventional toxicity studies is as follows: rat, 25 mg/kg/day; mouse, 20 mg/kg/day; hamster, 40 mg/kg/day; and monkey, 40 mg/kg/day/. However, a recent study conducted at the National Center for Toxicological Research revealed teratogenic effects in A/J mice at the lowest dose of commercial 2,4,5-T tested (15 mg/kg/day). It would appear, therefore, that there are strain differences in the no effect level for 2,4,5-T in mice.

Two three-generation studies of 2,4,5-T reproductive toxicity have been carried out in rats. One of these studies was carried out using commercial 2,4,5-T containing ≦0.05 ppm TCDD. No teratogenic effects, reproductive toxicity or fetal toxicity were observed in any animals at the doses tested (3, 10 and 30 mg/kg/day). In contrast another three-generation study carried out using purified 2,4,5-T (≦0.0003 ppm TCDD) reported a significant decrease in neonatal survival at 10 and 30 mg/kg/day but not at 3 mg/kg/day. However some effects suggestive of reproductive toxicity were noted at the intake level of 3 mg/kg/day in this study. The Scientific Advisory Panel believes that this three-generation study establishes for practical purposes a NOEL and recommends that this NOEL be used for subsequent evaluation of risk.

In summary, the Scientific Advisory Panel believes that these data suggest that a potential for reproductive risk and embryo toxicity exists for persons engaged in the mixing and application of commercial 2,4,5-T. However with use of protective clothing such as a one piece jump suit with long sleeves, gloves and, perhaps, respirators, risks should be reduced to an acceptable level. The potential for significant reproductive and teratogenic risk to persons living in the immediate area of the spraying operations does not appear to be substantial except as they may be directly exposed on a chronic basis.

The Panel has some reservations relative to the validity of the three-generation study in rats carried out by the Laboratory for Pharmakologie and Toxikologie using commercial 2,4,5-T (≦0.05 ppm TCDD), and recommends that an additional three-generation study in rats using commercial 2,4,5-T be carried out.

Silvex

Oncogenicity. The carcinogenic testing of commerical Silvex has been less extensive than with 2,4,5-T. However, those few studies which have been carried out did not indicate an increase in oncogenicity as a result of chronic exposure to Silvex. Although no carcinogenic risk has been demonstrated with commercial Silvex, these data must be viewed with some caution because of the contamination of commercial Silvex with TCDD.

Reproductive and Embryo Toxicity. In contrast to commercial 2,4,5-T, very few studies of the reproductive toxicity of Silvex have been carried out. Those studies with commercial Silvex that have been carried out in rats and mice indicate that commercial Silvex is teratogenic in mice at high doses (400 mg/kg/day). Silvex is also fetotoxic in mice and rats and the no effect level in rats is 25 mg/kg/day.

Thus commercial Silvex does appear to pose some risks to reproduction and fetal viability. Much less information is available concerning the degree of exposure of humans to Silvex during mixing and spraying operations than is the case with 2,4,5-T. However, it should also be possible using proper protective clothing to reduce the reproductive and teratogenic risk from commercial Silvex to an acceptable level. Similarly there does not appear to be any substantial risk to persons living in the immediate area of the spraying except from direct exposure on a chronic basis.

TCDD

Oncogenicity. Two major studies of the oncogenicity of TCDD have been reported. One study in rats has been carried out by the Dow Chemical Company and another in mice was performed by the Research Institute of Oncopathology in Hungary. A third study in mice and rats has recently been completed by NCI, but the results of this study were not yet available.

There was an increase in tumors of the liver, lung and hard palates/nasal turbinates in the rats fed of 0.1 ug/kg/day of TCDD in the diet. At a dose of 0.01 ug/kg/day there was an increase in hyperplastic nodules in the livers of the female rats. The EPA Carcinogen Assessment Group (CAG) has concluded that this increase in hyperplastic nodules at the dose of 0.01 ug/kg/day indicates that TCDD is also carcinogenic at this dosage level. The Scientific Advisory Panel concludes that there is a tumorigenic response at 0.01 ug/kg/day but has reservations as to whether hyperplastic nodules are precursors, *per se*, to hepatocellular carcinoma. (See Appendix II.)

An increased incidence of liver tumors were produced in studies in male outbred Swiss mice in which TCDD was given by gavage at a dose of 0.7 ug/kg/week for one year. However, in this study there was no significant increase in tumor formation in animals given TCDD at 7.0 ug/kg/day although there was a decreased life span in the mice receiving this dose. There was also no increase in tumors in animals given TCDD at a dose of 0.007 ug/kg/week. Evaluation of this study by the Scientific Advisory Panel is difficult, since the type of liver tumor produced was not identified. Although the authors stated that the ratio of benign hepatomas to hepatocellular carcinomas was the same in the animals receiving the 0.7 ug/kg/week dose of TCDD as in the controls, it is not clear whether there was a significant increase in hepatocellular carcinomas in the treated animals.

The Scientific Advisory Panel concludes that there is a level of TCDD below which no oncogenic or tumorigenic effects were seen in either mice or rats. The dose level for tumorigenic response in the outbred strain of Swiss mice used in the Hungarian oncogenic study lies between 0.007 and 0.7 ug/kg/week. The Scientific Advisory Panel believes that the data available from this study are insufficient to reach a firm conclusion regarding whether there was a true oncogenic response in mice. In rats there was some controversy over which level of exposure to TCDD demonstrated an oncogenic effect. The Dow Chemical Company scientists stated that the level at which no oncogenic effects are seen lies between a dose of 0.1 and 0.01 ug/kg/day in the diet. The EPA Carcinogen Assessment Group concluded that the non-oncogenic dose lies between 0.01 and 0.001 ug/kg/day. Thus, there was agreement concerning the lack of an oncogenic response at the dose level of 0.001 ug/kg/day TCDD.

The major concern of the Scientific Advisory Panel relative to the potential oncogenic risk from TCDD is whether TCDD accumulates in the human food chain. The data necessary to evaluate this risk must be derived from monitoring data for TCDD itself. The oncogenic risk from TCDD present as a contaminant in commercial 2,4,5-T and Silvex is best determined in those experiments in which commercial 2,4,5-T or Silvex contaminated with TCDD has been administered chronically to rats and mice.

The monitoring data obtained thus far does not suggest that TCDD derived from commercial 2,4,5-T and Silvex exhibits any tendency to accumulate in the human food chain in amounts which would pose a substantial risk. For example TCDD has been detected in some fat samples from cows grazed on rangeland immediately after spraying with commercial 2,4,5-T and sacrificed 2 weeks later. If one assumes that all beef fat in the U.S. contains TCDD at the level found in these studies (approximately 10 ppt) and if one assumes further that the average level of beef intake in the U.S. Population is 6% of the diet; (1.5 kg food/day, 15% of beef is fat) and produces a 22% incidence of tumors at 0.1 ug/kg/day (Dow Study) a risk of 4×10^{-6} can be calculated. It should be pointed out that this is an extreme worse case calculation since the present data indicate that only a small percent (approximately 7%) of beef fat samples from animals fed on ranges immediately after spraying with 2,4,5-T containing TCDD and that all beef eaten in the U.S. does not come from ranges sprayed with 2,4,5-T (only 2%). Thus, although it appears that there is some potential oncogenic risk from TCDD present in the food chain, on the basis of the current

monitoring data, the risk is judged to be small.

Reproductive Toxicity. The results of the embryo toxicity studies indicate that the no effect level for TCDD in mice is 0.1 ug/kg/day (days 6-15 of gestation), in rats is 0.03 ug/kg/day (days 6–15 of gestation), and in monkeys is 0.02 ug/kg/3 times per week (days 20–40 of gestation).

In a three-generation reproductive study carried out in rats by the Dow Chemical Company clear cut embryo toxicity was seen at doses of 0.1 and 0.01 ug/kg/day of TCDD. At the dose of 0.001 ug/kg/day there was a decreased gestational survival in the F_2 generation but not in earlier or later generations. Postnatal survival in the group receiving 0.001 ug/kg/day was decreased in the F_{1a} generation and increased in the F_{1b} generation relative to the controls. An increase in dilated renal pelvis was also seen in the F_{1a} and F_{1b} generation in the animals receiving 0.001 ug/kg/day but not in later generations or at the 0.01 ug/kg/day dose. Although these effects at 0.001 ug/kg/day are suggestive of an embryo-toxic effect, the inconsistency of the effects from generation to generation and in relation to the higher dose of 0.01 ug/kg/day (dilated renal pelvis) suggests that the 0.001 ug/kg/day dose is for all practical purposes a no effect level.

Long term studies in monkeys have shown reproductive toxicity from TCDD at levels of 50 ppt in the diet. Studies are currently underway at 25 ppt of TCDD in the diet, but results are not yet available. An intake of TCDD of 50 ppt in the diet is equivalent to approximately 0.002 ug/kg/day. If no reproductive toxicity is seen in the monkeys exposed to TCDD in the diet at 25 ppt, then the no effect level in the monkey will be similar to that seen in the rat, namely about 0.001 ug/kg/day.

The major concern of the Scientific Advisory Panel relative to the potential reproductive toxicity or teratogenic effects of TCDD is whether it accumulates in human food chains as previously noted for the oncogenic potential of TCDD. The reproductive toxicity and teratogenic potential of TCDD present as a contaminant in commercial 2,4,5-T and Silvex is best determined from experiments in animals exposed to commercial 2,4,5-T or Silvex contaminated with TCDD.

If one assumes the worse case situation decribed previously in the evaluation of the oncogenic risk from TCDD in which TCDD is proposed to be present in the fat of all cows marketed in the U.S., the maximum intake would be approximately 2×10^{-8} ug/kg/day. Using a 0.001 ug/kg/day as the no effect level the safety factor would be approximately 500. As pointed out previously in the section on the oncogenicity of TCDD, this calculation represents an extreme exaggeration of exposure to TCDD. The Scientific Advisory Panel believes, therefore, that the current monitoring data do not indicate that there is a substantial reproductive or teratogenic risk posed by the accumulation of TCDD in the human food chain.

Appendix II.—A Selected Review of the Histology of the Dow TCDD Study (Tox. Appl. Pharm. 46, 279 (1978))

Drs. Doana Kuroda, Richard Kociba and I reviewed 3 representative microscopical sections each from control, 0.01, and 0.1 μg/kg/day level TCDD exposed female Sprague Dawley rats. These sections were selected by Dr. Kociba to demonstrate hyperplastic nodules and lesions designated hepatocellular cancers [see Table #5 R. J. Kociba et al. Tox. & Appl. Pharm. *46*, 279 (1978)]. Control sections were used for comparison.

Control animals, selected from timed sacrifices, showed a general presentation of the liver architecture. A natural incidence (spontaneous?) of extramedullary hematopoiesis, bile duct reduplication, and "hyperplastic nodules" was found by Dr. Kociba (Table 5) and demonstrated in the sections provided to me. Kociba and colleagues considered a tissue mass to represent a hyperplastic nodule if a group of liver cells, with or without sinusoidal lining cells, formed a discrete population with cellular structure and/or tinctorial properties different from the surrounding parenchyma. These growths may or may not cause compression of surrounding parenchyma and may or may not have bile duct formation. Sharp demarcation from the surrounding parenchyma was observed.

In addition, there were both acute inflammatory exudates and granuloma-like lesions in the controls, not associated with the hyperplastic nodule. In addition there appeared to be an acute cholangitis. No evidence of fibrosis was present.

Sections from the high dose exposure animals (0.1 μg/kg/day) showed some distortion of the hepatic parenchyma with cellular variability and thickening of the liver cell plates. Portal tracts were sometimes associated with dense collections of lymphocytes. Prominent were hyperplastic nodules and lesions characterized by Kociba and associates as hepatocellular carcinomata. These latter lesions showed more marked cellular differences from surrounding parenchyma and from hyperplastic nodules. In general, the liver cell nuclei were larger occupying a greater portion of the cell volume, the cell plates more disordered, formation of acinar and tubular forms were identified, and no formation of portal tracts were present in these lesions. These masses in one instance, arose in a hyperplastic nodule. No defined microscopical or gross evidence of invasion of the neoplastic cells into adjacent tissues was noted either at autopsy (according to Kociba) or by microscopy. Not infrequently fat was present in hyperplastic nodules but not in the "carcinomata."

The parenchyma adjacent to the carcinomatous and hyperplastic nodules showed some cellular irregularity, staining variation, and hyaline intracytoplasmic masses. No significant evidence of increased inflammatory exudates or fibrosis was noted, but bile duct reduplication was present.

The midrange dose shows hyperplastic nodules, the remaining changes were identical with the high dose, but these slides did not show a carcinoma. I believe that the group at Dow extensively and properly surveyed the evidence of hepatocellular disease following exposure of rats to TCDD. Autopsies on animals were conducted by pathologists and tissue sections were selected by them. Their microscopial review was extensive. Their nomenclature was defined and understandable. I personally would have been more conservative than they in designating carcinomata, so their result is a "worst case" designation. From these discussions and reviews, I am very comfortable with their evaluation for toxic injury and carcinogenesis. Additionally, I believe liver cancer was shown in the high dose level; might be questioned in the midrange level, but was not present in the low dose group.

Edward Smuckler,

Professor and Chairman, Department of Pathology, University of California School of Medicine, San Francisco, Calif.

August 15, 1979.

Survey conducted at EPA Headquarters, 401 M Street SW., Washington, D.C. 20460

Appendix C.—Department of Agriculture, Office of the Secretary

August 10, 1979.

Mr. Edwin L. Johnson,

Deputy Assistant Administrator for Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C. 20460.

Dear Ed: The Secretary has asked me to respond to your letter of July 9, 1979, regarding the proposal to hold hearings under Section 6(b)(2) of the Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. 136d(b)(2) to determine whether or not the nonsuspended uses of 2,4,5-T and silvex should be cancelled.

As you know, the Secretary is a party on the Section 6(b)(1) hearing. Except for slightly different use patterns and exposure considerations, the issues on both the suspended and nonsuspended uses are similar and we, therefore, plan to participate in the 6(b)(2) portion as well.

Contrary to statements in the Notice of Intent to hold a hearing on the remaining uses of silvex, the Department of Agriculture has not provided information on the "social, economic, and environmental benefits" of using silvex to you. This information is currently being collected by the joint USDA/States/EPA assessment team, but since an RPAR notice was not issued on this compound, the team, which was organized recently, has only had time to develop some preliminary data.

We agree that it is in the best interest of everyone to attempt to resolve all issues in a consolidated hearing. We are preparing to have information available on all uses of both 2,4,5-T and silvex for presentation to the Administrative Law Judge during these proceedings.

We will be submitting for the record of the hearings the benefit and exposure information contained in the 2,4,5-T assessment report prepared by the joint USDA/States/EPA assessment team as well as information presently being gathered by the joint assessment team on silvex. We believe that the assessment team activity has

been an effective means for assembling information needed in the regulatory decision process.

Your notice indicates that additional data on the benefits of the recommended uses of 2,4,5-T will be needed before a final regulatory decision can be made. It would be most helpful to us and to the process if you would point out specifically where the data in the OSTA/Hazelton/EPA report "The Biologic Economic Assessment of 2,4,5-T" is not adequate. We are anxious to cooperate with you to fill any data gaps that may exist to ensure that all possible information can be considered in reaching a final decision.

Sincerely,

Barry R. Plunkett,

Director, Office of Environmental Quality.

[FR Doc. 79-38978 Filed 12-12-79; 8:45 am]

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