Overview of the 2,4-D Risk Assessments

June 18, 2004

Introduction

This document summarizes EPA's human health and ecological risk findings and conclusions for the herbicide 2,4-dichlorophenoxyactic acid (2,4-D), as presented fully in the documents, *2,4-D. HED's Human Health Risk Assessment for the Reregistration Eligibility Decision (RED) Revised to Reflect Error-only Comments from Registrants*, dated June 2, 2004, and the *Environmental Fate and Effects Division's Risk Assessment for the Reregistration Eligibility Document for 2,4- Dichlorophenoxyacetic Acid (2,4-D)*, dated May 24, 2004. These documents also summarize the HED and EFED response to comments as submitted by the registrants and the 2,4-D Task Force, during Phase I of the Public Participation Process. The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments and conclusions reached in the assessments. This overview was developed in response to comments and requests from the public which indicated that the risk assessments were difficult to understand, that they were too lengthy, and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

The risk assessments for 2,4-D will be made available to the public in EPA's Pesticide Docket, and will be posted on the Internet. Once the risk assessments are available to the public, there will be an opportunity for the public to view them and to comment on them. Public comments will be invited and welcomed. This feedback will be used to complete the Reregistration Eligibility Decision (RED) document, which will include the resultant risk management decisions. These documents, in hard copy form, may be viewed in the OPP docket room and public comments may be submitted to the OPP public docket under **OPP-2004-0167**, located in Room 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA or viewed via the Internet and public comments may be submitted to the OPP electronic docket at: www.epa.gov.edockets under the same docket number. In addition, documents may be downloaded or viewed via the Internet at: www.epa.gov/pesticides/reregistration/.

Use Profile

- **Herbicide:** 2,4-D is a herbicide in the phenoxy family used for selective control of broadleaf weeds. 2,4-D, a synthetic auxin herbicide, causes disruption of plant hormone responses. Plant injuries include growth and reproduction abnormalities, especially on new growth. Symptoms may appear on young growth almost immediately after application, but death may not occur for several weeks. 2,4-D formulations are typically applied as broadcast, banded, or directed (spray or wiper) applications during dormancy or preplant, preharvest, preemergence, emergence, postemergence, or postharvest using ground or aerial equipment. Registered forms of 2,4-D incude 2,4-D acid, 2,4-D

dimethylamine salt (DMAS), 2,4-D isopropyl acid (IPA), 2,4-D triisopropyl acid (TIPA), 2,4-D ethylhexyl ester (EHE), 2,4-D butoxy ethyl ester (BEE), 2,4-D diethyl amine (DEA), 2,4-D isopropyl ester (IPE), and 2,4-D sodium salt.

- **Use Sites:** In terms of pounds, total 2,4-D usage is allocated mainly to pasture/rangeland (24%), lawn by homeowners with fertilizer (12%), Spring wheat (8%), Winter wheat (7%), lawn/garden by lawn care operators/landscape maintenance contractors (7%), lawn by homeowners alone (without fertilizer) (6%), field corn (6%), soybeans (4%), summer fallow (3%), hay other than alfalfa (3%) and roadways (3%). Agricultural sites with at least 10% of U.S. acreage treated include Spring wheat (51%), filberts (49%), sugarcane (36%), barley (36%), seed crops (29%), apples (20%), rye (16%), Winter wheat (15%), cherries (15%), oats (15%), millet (15%), rice (13%), soybeans (12%) and pears (10%).

- **Tolerances:** Tolerances are currently established for residues of 2,4-D in/on: numerous raw agricultural commodity (RAC) human foods derived from fruits, grasses, grains, nuts, vegetables, sugarcane, cotton, hops, and asparagus at 0.1 ppm to 5 ppm; processed products of sugarcane (5 ppm) and grains (2 ppm); fish and shellfish at 1.0 ppm and potable water at 0.1 ppm [40 CFR §180.142(a)(1-6 and 9-13)]. A temporary tolerance of 0.02 ppm for 2,4-D per se in/on soybean seed will expire on 12/31/04 [40 CFR §180.142(a)(11)]. A time-limited tolerance of 0.1 ppm in/on wild rice established under FIFRA Section 18 will expire 12/31/05. Tolerances for residues in livestock commodities are currently established in terms of residues of 2,4-D and/or its metabolite 2,4-dichlorophenol [40 CFR §180.142(a)(8)].

- **Formulations:** Formulation types registered include emulsifiable concentrate, granular, soluble concentrate/solid, water dispersible granules (dry flowable), and wettable powder.

- **Method of Application:** 2,4-D may be applied with a wide range of application equipment including aircraft, backpack sprayer, band sprayer, boom sprayer, granule applicator, ground, hand held sprayer, helicopter; injection equipment, tractor-mounted granule applicator, and tractor-mounted sprayers. Methods of application of 2,4-D may include band treatment, basal spray treatment, broadcast, frill treatment, girdle treatment, ground spray, soil band treatment, soil broadcast treatment, spot treatment, stump treatment, tree injection treatment, and water related surface treatment.

- **Use Rates:** For 2,4-D, rates per application and rates per year are generally less than or equal to 1.50 pounds acid equivalents (ae) per acre (lbs ae/A) and 2.00 lbs ae/A, respectively.

- **Annual Poundage:** Based primarily on pesticide usage information from 1992 through 2000 for agriculture and 1993 through 1999 for non-agriculture, total annual domestic usage of 2,4-D is approximately 46 million pounds, with 30 million pounds (66%) used by agriculture and 16 million pounds (34%) used by non-agriculture. 2,4-D is used predominantly in the Midwest, Great Plains, and Northwestern United States.

- **Technical Registrants:** Industry Task Force II on 2,4-D Research Data. Members include: Agro-Gor Corp (jointly owned by Attanor, S.A. and PBI-Gordon Corp.), Dow AgroSciences, and Nufarm USA.

Human Health Risk Assessment

In laboratory animals, following subchronic, oral exposure at dose levels of 2,4-D above the threshold of saturation for renal clearance, the primary target organs are the eye, thyroid, kidney, adrenals, and ovaries/testes. 2,4-D is classified as a Group D chemical (not classifiable as to human carcinogenicity). 2,4-D acid is currently considered to be representative of all nine member chemicals of the 2,4-D case.

Acute Dietary (Food) Risk

(For a compete discussion, see section 3.0 of the Human Health Risk Assessment)

Acute dietary risk is calculated considering what is eaten in one day and maximum, or high-end residue values in food. A risk estimate that is less than 100% of the acute Population Adjusted Dose (aPAD), the dose at which an individual could be exposed on any given day and no adverse health effects would be expected, does not exceed the Agency's level of concern. The aPAD is the acute reference dose (aRfD) adjusted for the FQPA Safety Factor.

- Acute dietary (food) risks are all less than the Agency's level of concern (i.e., less than 100% of the aPAD). Acute dietary risks were calculated using both Lifeline and DEEM software. Lifeline and DEEM are computer models that calculate estimated exposure concentrations.
- For females 13-50 years of age, the toxicological endpoint is skeletal abnormalities as seen at the lowest observed adverse effect level (LOAEL) of 75 mg/kg/day in the rat developmental toxicity study The no observed adverse effect level (NOAEL) in this study is 25 mg/kg/day.
- For the general population including infants and children, the toxicological endpoint is gait abnormalities as seen at the lowest observed adverse effect level (LOAEL) of 227 mg/kg/day in the acute neurotoxicity study in rats. The no observed adverse effect level (NOAEL) in this study is 67 mg/kg/day.
- Risk to the general U.S. population was 17% of the aPAD using both DEEM and Lifeline.
- The most highly exposed population subgroup using both DEEM and Lifeline was children 1-2 years of age; risks were 33% and 30% of the aPAD, respectively.
- Although not the most highly exposed population subgroup, risk to females 13-49 years of age was 31% of the aPAD using DEEM and 42% of the aPAD using Lifeline; these higher risks are due to the 2.7x lower NOAEL for developmental effects applicable to the acute dietary risk assessment of Females 13-49 years of

age.

- A 10x database uncertainty factor has been assessed based on the need for a developmental neurotoxicity study in the rat, and a 2-generation reproduction study with special emphasis on thyroid and immunotoxic effects.

Chronic Dietary (Food) Risk

(For a compete discussion, see section 3.0 of the Human Health Risk Assessment)

The chronic dietary assessment was moderately refined, making use of the following: tolerance-level exposure values for most commodities; averages of field trial data and processing study factors for small grains, citrus, and sugarcane sugar and molasses; % crop treated (CT) information for all commodities; and the MCL (70 ppb) as well as the highest observed groundwater monitoring concentration (15 ppb) for drinking water in a forward calculation. As in the case of the acute assessment, one-half the value for the average limit of detection (LOD) from PDP monitoring data was used for milk.

- Chronic dietary risks are all less than the Agency's level of concern (i.e., less than 100% of the aPAD).
- The toxicological endpoints are decreased body-weight gain (females) and food consumption (females), alterations in blood cell and blood chemistry parameters, increased thyroid weights (both sexes), and decreased testes and ovarian weights, as seen at the lowest observed adverse effect level (LOAEL) of 75 mg/kg/day in the rat chronic toxicity study. The no observed adverse effect level (NOAEL) in this study is 5 mg/kg/day.
- For food consumption only, chronic dietary (food only) risks calculated using the DEEM software consumed 2.5-6.9% of the cPAD (2.5-6.7% cPAD using Lifeline).
- Risk to the general U.S. population was 3.4% of the cPAD using DEEM and 3.2% cPAD using Lifeline.
- Risk to children 1-2 years of age, the most highly exposed population subgroup, was 6.9% of the cPAD using DEEM and 6.7% cPAD using Lifeline.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. To determine the maximum allowable contribution from water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by food and then determines a "drinking water level of comparison" (DWLOC) to ascertain whether modeled or monitored concentration levels exceed this level.

The Agency uses the DWLOC calculation to estimate risk associated with exposure from

pesticides in drinking water. The DWLOCs represent the maximum contribution to the human diet (in ppb or ug/L) that may be attributed to residues of a pesticide in drinking water after dietary exposure is subtracted from the aPAD or the cPAD. Risks from drinking water are assessed by comparing the DWLOCs to the estimated environmental concentrations (EECs) in surface water and groundwater. EECs less than the DWLOC are not of concern. Drinking water modeling is considered to be an unrefined assessment and generally provides high-end estimates.

For the current assessment, EECs were derived through an evaluation of monitoring data and modeling. A number of different scenarios were assessed and EECs provided for each. Scenarios evaluated included the direct application of 2,4-D to water bodies for aquatic weed control, a rice use scenario, and terrestrial uses including food and nonfood uses. Although of high quality, the available monitoring data is not targeted to 2,4-D use. However, the data provide context to model results and indicate that there is little evidence that concentrations are likely to be found exceeding these estimates. In addition, several registrant-submitted aquatic dissipation studies provide additional context to the scenarios discussed below.

- **Acute water risk:**
  - The lowest acute DWLOC is 450 ppb for children 1-2 years old which is higher than the estimated drinking water concentration (EDWC) of 70 ppb (aquatic weed control), 118 ppb (terrestrial use, or 280 ppb (calculated from MCL) applicable to surface water, as well as the groundwater EDWC of 15 ppb.
  - If it is determined that for aquatic weed contol use, the 70-ppb label restriction is practical, enforceable, and uniformly-applied, acute aggregate risk estimates associated with exposure to 2,4-D residues in food and drinking water do not exceed HED's level of concern. However, if the opposite determination is made, the modeled peak concentration of 811 ppb is above the DWLOCs calculated for infants, children, and females 13-49 years old, thus creating at least an apparent risk that exceeds the Agency's level of concern.

- **Chronic water risk:** DWLOCs were not calculated for the chronic aggregate assessment because, as per recent policy, drinking water exposure to 2,4-D is included directly in the overall dietary risk using the DEEM and Lifeline software to generate a quantitative aggregate assessment.

Dermal and Inhalation Toxicity

The following endpoints were used to determine residential, aggregate, and occupational risk.

- Short-term incidental oral, dermal, and inhalation exposures: LOAEL of 75 mg/kg/day and NOAEL of 25 mg/kg/day, based on decreased maternal body-weight gain and skeletal malformations and skeletal variations from the rat developmental toxicity study.
- Intermediate-term and long-term incidental oral, dermal, and inhalation exposures are not expected based on the 2,4-D use scenarios.

Note that the dermal absorption rate, as determined from a human dermal absorption study, is 5.8% of that absorbed via the oral route for all dermal exposure durations. As there is no available repeat-dose 2,4-D inhalation study, absorption via the inhalation route is assumed to be equivalent to oral absorption, i.e., 100%. All of the above exposure routes and durations are applicable to the residential setting. A 10x database uncertainty factor has been assessed based on the need for a developmental neurotoxicity study in the rat, and a 2-generation reproduction study with special emphasis on thyroid and immunotoxic effects. Therefore, the target residential MOE = 1000 for assessment of incidental oral, dermal, and inhalation risks.

Residential Risk

(For a complete discussion, see section 4.4 of the Human Health Risk Assessment)

According to the EPA Pesticide Sales and Usage Report for 1998/1999, 2,4-D is the most commonly used conventional pesticide active ingredient in the home and garden market sector with 7 to 9 million pounds applied per year. It is also the most commonly used conventional active ingredient in the Industry/Commercial/Government market section with 17 to 20 million pound applied per year. This segment includes applications to homes and gardens by professional applicators.

- The residential products are typically formulated as dry weed and feed products or as liquids in concentrates or ready to use sprays.
- Many of these formulations include other phenoxy herbicides such as MCPP-p and dicamba.
- Both spot and broadcast treatments are included on the labels. Exposures are expected to be short-term in duration for broadcast treatments because the label allows only two broadcast treatments per year. Exposures are also expected to be short-term in duration for spot treatments because the labels recommend repeat applications for hard to kill weeds in two to three weeks.

Residential Applicator (Handler)

- A summary of the MOE calculations for homeowner lawn applicators is included in Table 1. All of the MOEs are greater than the target MOE of 1000 and are not of concern.

Table 1. 2,4-D Short-term MOEs for Homeowner Applications to Lawns

Scenario	Application Rate (lbs ae/acre)	Treated Area (acres/day)	MOE
1 Hand Application of Granules	2.0	0.023	4,600
2 Belly Grinder Application	2.0	0.023	5,100
3. Load/Apply Granules with a Broadcast Spreader	2.0	0.5	38,000
4. Mix/Load/Apply with a Hose-end Sprayer (Mix your own)	2.0	0.5	2,300
5. Mix/Load/Apply with a Hose-end Sprayer (Ready to Use)	2.0	0.5	9,300
6. Mix/Load/Apply with Hand Held Pump Sprayer	2.0	0.023	15,000
7. Mix/Load/Apply with Ready to Use Sprayer	2.0	0.023	10,000
Note: 1000 square feet equals 0.023 acres			

Residential Postapplication-Turf Use

- MOEs resulting from both short-term (California turf transferrable residue (TTR) data only) and one-day toddler postapplication exposures (i.e., hand-to-mouth, object-to-mouth, and soil ingestion) to treated turf were 1000, just matching the Agency's level of concern. In the case of adults, the one-day/short-term postapplication exposure MOEs were 1300 for heavy yardwork and 19000 for playing golf: neither scenario is of Agency concern.

Residential Postapplication-Aquatic Use

The master label indicates that 2,4-D can be used for aquatic weed control of surface weeds such as Water Hyacinth and submersed weeds such as Eurasian Milfoil. Surface weeds are controlled by foliar spray applications at a maximum rate of 2.0 lb ae/acre. Submersed weeds can be controlled by subsurface injection of liquids to achieve a target concentration of 2 to 4 ppm in the water column surrounding the weeds. Although many herbicide treatments are applied to aquatic areas where recreational swimming is not likely to occur, some of the subsurface treatments are made at recreational lakes. These treatments are made because the Eurasian Milfoil interferes with recreation and other activities. This problem is particularly prevalent in northern states such as Minnesota, Pacific Northwest states such as Washington, and in the New England region.

- Potential post-application residential exposure scenarios that result from the aquatic use of 2,4-D include dermal exposure and incidental ingestion of water.
- All of the dermal MOEs meet or exceed the target MOE of 1000, and are thus not of concern, when 2,4-D acid or 2,4-D DMA is used, because these forms have very low skin permeability coefficients.
- Both the one-day and short-term dermal MOEs are of concern when 2,4-D BEE is used because 2,4-D BEE has a relatively high skin permeability coefficient.
- The ingestion MOEs are of concern for short-term children's exposure and are not dependent on the form used.
- If a lower target concentration of 2 ppm is used, the MOEs for ingestion rise to above 1000; however, the dermal MOEs remain below 1000 for 2,4-D BEE exposures.

Aggregate Risk

(For a complete discussion, see section 5.0 of the Human Health Risk Assessment)

Aggregate risk looks at the combined risk from exposure through food, drinking water, and residential uses of a pesticide. Generally, all risks from these exposures must occupy less than 100 percent of the PAD to be below the Agency's level of concern.

For aggregate risk, EPA considers the combined exposures from food and residential sources and calculates a DWLOC (as described above in the drinking water section) which represents the maximum allowable exposure through drinking water after considering the food and residential exposures. If the water estimated environmental concentrations (EECs) are less than the DWLOCs, EPA does not have concern for aggregate exposure. As noted above, DWLOCs were not calculated for the chronic aggregate assessment because, as per recent policy, drinking water exposure to 2,4-D is included directly in the overall dietary risk using the DEEM and Lifeline software to generate a quantitative aggregate assessment.

Aggregate risk assessments for 2,4-D were conducted as follows: acute and chronic aggregate assessments were conducted based on food and water exposures and one-day, short-term, and intermediate-term aggregate assessments were conducted based on food, water, and residential exposures. No long-term aggregate risk assessment was conducted because no long-term exposure scenarios are expected from residential uses of 2,4-D.

Acute Aggregate

To estimate aggregate acute risks, DWLOCs were calculated. Table 2 summarizes the acute DWLOCs calculated for the various population subgroups indicated.

- The lowest acute DWLOC is 450 ppb for children 1-2 years old which is higher than the EDWC of 70 ppb, 118 ppb, or 280 ppb applicable to surface water as well

as the groundwater EDWC of 15 ppb, and therefore, does not exceed EPA's level of concern. If it is determined that the 70-ppb label restriction is practical, enforceable, and uniformly-applied, acute aggregate risk estimates associated with exposure to 2,4-D residues in food and drinking water would not exceed HED's level of concern.

- However, if the opposite determination is made, and a 1500 ft set back restriction was added to the label, the modeled peak concentration of 811 ppb is above the DWLOCs of 450-540 ppb calculated for infants, children, and females 13-49 years old, thus creating at least an apparent risk that exceeds the Agency's level of concern.

Table 2. Acute DWLOC Calculations.

Population Subgroup	aPAD (mg/kg/day)	Food Exp (mg/kg/day)	Max Water Exp (mg/kg/day[a])	Ground Water EEC (µg/L)	Surface Water EEC (µg/L)	DWLOC (μg/L)[b]
General U.S. Population	0.067	0.011710	0.055290	15	70 (aquatic) or 118 (terrestrial) or 240 (calculated from MCL)	1900
All Infants (< 1 year old)		0.012766	0.054234			540
Children 1-2 years old		0.022134	0.044866			450
Children 3-5 years old		0.020610	0.046390			460
Children 6-12 years old		0.014632	0.052368			520
Youth 13-19 years old		0.009140	0.057860			1700
Adults 20-49 years old		0.008645	0.058355			2000
Adults 50+ years old		0.006563	0.060437			2100
Females 13-49 years old	0.025	0.007675	0.017325			520

[a] Maximum water exposure (mg/kg/day) = [(acute PAD (mg/kg/day) - food exposure (mg/kg/day)]

[b] DWLOC (μg/L) = [maximum water exposure (mg/kg/day) x body weight (kg)] ÷ [water consumption (L) x 10^{-3} mg/μg]. Consumption = 1 L/day for populations <13 years old and 2 L/day for populations ≥ 13 years old. Default body weights = 70 kg for adults > 20 years old and general U.S. population, 60 kg for females ≥ 13 years old and youth 13-19 years old, and 10 kg for all others. Values are rounded to 2 significant figures.

Chronic Aggregate

If both the 1500-ft setback and the 70-ppb maximum limit on the Task Force II Master Label are present on all aquatic use labels and if both of these restrictions are determined to be practical, enforceable, and universally-applied, then chronic dietary exposure to 2,4-D (food plus water sources) leads to risks that are less than the Agency's level of concern (100% of the cPAD) for all population subgroups reflecting food plus drinking water residues.

One-day/Short-term Aggregate

One-day and short-term risk estimates associated with exposure to 2,4-D residues on

lawns and via recreational activities (swimming or golfing) exactly meet or exceed HED's level of concern (MOE's $\leq$1000) for the following scenarios:

- toddlers exposed postapplication to 2,4-D-treated lawns (MOE = 1,000 for one scenario);
- adults swimming in 2,4-D BEE-treated water (MOE = 310);
- 22-kg child swimming in 2,4-D acid- and 2,4-D DMA-treated water (MOE = 920); and
- 22-kg child swimming in 2,4-D BEE-treated water (MOE = 220).
- All of these one-day and short-term residential or recreational risks alone are either of Agency concern (i.e., MOEs are less than the target of 1000) or they just meet the target MOE of 1000 and would be of Agency concern if additional 2,4-D exposure due to consumption of food or drinking water were aggregated.

Occupational Risk

(For a compete discussion, see section 7.0 of the Human Health Risk Assessment)

Workers can be exposed to a pesticide through mixing, loading, or applying the pesticide, and reentering a treated site. Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to the NOAEL taken from animal studies. Generally, MOEs that are greater than 100 do not exceed the Agency's level of concern.

The following assumptions and factors were used in order to complete the exposure and risk assessments for occupational handlers/applicators:

- The average work day was 8 hours.
- A listing of application methods and amounts of acreage treated per 8 hour day is included in Table 17.
- The application rate for submerged aquatic weeds is based upon the master label rate of 10.8 lbs a.i. per acre foot times an average lake depth of 5 feet.
- Maximum application rates and daily acreage were used to evaluate short term exposures.
- Average application rates were used to evaluate intermediate term exposures.
- A body weight of 60 kg was assumed for short-term exposures because the short-term endpoint relates to females 13-50 years of age.
- A body weight of 70 kg was assumed for intermediate-term exposures because the intermediate-term endpoint is not gender-specific.
- The dermal absorption rate is 5.8%.
- The inhalation absorption rate is 100%.
- Baseline PPE includes long sleeve shirts, long pants and no gloves or respirator.
- Single Layer PPE includes baseline PPE with gloves.
- Double Layer PPE includes coveralls over single layer PPE
- Double Layer PPE PF5 includes above with a PF5 respirator (i.e. a dustmask)
- Double Layer PPE PF10 includes above with a PF10 cartridge respirator

- Only closed cockpit airplanes are used for aerial application.
- There are very few exposure data to evaluate the exposure in rotary-winged aircraft; therefore, the exposure data for fixed-wing aircraft are used as a surrogate.
- Airplane and helicopter pilots do not wear chemical resistant gloves.

Based on currently registered use sites, formulations, and types of equipment commonly used for mixing, loading, and application, EPA has identified 18 major occupational handler scenarios.

- With the exception of mixing/loading wettable powder, the short-term and intermediate-term MOEs are greater than the target of 100 with baseline or single layer PPE and are not of concern. The MOEs for handling wettable powder are greater than 100 with engineering controls (i.e. water-soluble bags).
- The labels typically require single-layer PPE for applicators and handlers and that a mechanical system (probe and pump or spigot) be used for containers of 5 gallons or more. The mechanical system is not required for 1 to 5 gallon containers; however, additional PPE (coveralls or a chemical resistant apron) are required if the mechanical system is not used.
- Most of the wettable powder products are packaged in water-soluble bags.

Occupational Postapplication Exposures and Risk

To provide weed control without damaging crops, 2,4-D applications are made during the dormant season or prior to planting, sprays are directed to the row middles or orchard floors, and drop booms and/or shields are used to prevent crop foliar contact. These techniques also reduce postapplication exposures because they minimize the amount of residue on the crop foliar surfaces. However, broadcast applications may be made to grass crops such cereal grains, rice and sugarcane which are tolerant of 2,4-D.

- Given the above characteristics of 2,4-D, it is anticipated that postapplication exposures would primarily occur following broadcast treatment of grass crops. Because 2,4-D is typically applied only a few times per season and because the agricultural scenarios occur for only a few months per year, it is anticipated that 2,4-D exposures would primarily be short-term and secondarily intermediate-term.
- Potential inhalation exposures are not anticipated for the postapplication worker scenarios because of the low vapor pressure of 2,4-D (2.0e-07 torr at 20^{o} C).
- For postapplication occupational exposures, all of the short-term MOEs are above 100 on day zero which indicates that the risks are not of Agency concern. The intermediate-term MOEs are also all above 100 on day zero and are not of Agency concern.

In the Worker Protection Standard (WPS), a restricted entry interval (REI) is defined as the duration of time which must elapse before residues decline to a level such that entry into a

previously treated area and performance of a specific task or activity would not result in exposures that are of concern.

- The WPS REI for 2,4-D, based on acute toxicity, is 12 hours for the ester and sodium salt forms and is 48 hours for the acid and amine salt forms.

Ecological Risk

To estimate potential ecological risk, EPA integrates the results of exposure and ecotoxity using the risk quotient method. Risk quotients (RQs) are calculated by dividing exposure estimates by ecotoxity values, both acute and chronic, for various wildlife species. RQs are then compared to levels of concern (LOCs) to assess the potential for adverse ecological effects. Exceedance of an LOC indicates potential risk to nontarget organisms and the need for the Agency to consider mitigation measures. Risk characterization provides further information on the likelihood of adverse effects occurring by considering the fate of the chemical in the environment, communities and species potentially at risk, their spatial and temporal distributions, and the nature of the effects observed in studies. Generally, the higher the RQ the greater the potential risk. Reported incidents to nontarget organisms, such as fish and birds, involving the use of a pesticide can provide meaningful information to confirm the results of risk assessments and to help characterize ecological risks.

Environmental Fate and Transport

(For a complete discussion, see the Environmental Fate and Ecological Risk Assessment.)

2,4-D acid is non-persistent to moderately persistent in aerobic, aquatic, and terrestrial environments under laboratory and field conditions, is persistent in anaerobic aquatic environments, and is mobile in soil and aquatic environments.

The Agency proposed an environmental fate bridging strategy in the 1988 Registration Standard for the amine salts and esters of phenoxy herbicides, and also proposed that studies conducted with the acid provide "surrogate data" for 2,4-D amine salts and esters. The Agency required submission of data providing information on the dissociation time of 2,4-D amine salts and rate of hydrolysis of 2,4-D esters as confirmatory data for this strategy. Currently the Agency has received bridging data for 2,4-D DMAS, 2,4-D IPA, 2,4-D TIPA, 2,4-D EHE, 2,4-D BEE, 2,4-D DEA, 2,4-D IPE and 2,4-D sodium salt. The bridging data indicate esters of 2,4-D are rapidly hydrolyzed in alkaline aquatic environments, soil/water slurries, and moist soils. The 2,4-D amine salts have been shown to dissociate rapidly in water. However, 2,4-D esters may persist under extremely dry soil conditions and sterile acidic aquatic conditions.

The weight of evidence from open-literature and registrant-sponsored data, reviewed

subsequent to establishment of the bridging strategy, indicates that 2,4-D amine salts and 2,4-D esters are not persistent under most environmental conditions including those associated with most sustainable agricultural conditions. 2,4-D amine salt dissociation is expected to be instantaneous (< 3 minutes) under most environmental conditions. Although the available data on de-esterification of 2,4-D ester may not support instantaneous conversion from the 2,4-D ester to 2,4-D acid, it does show 2,4-D esters in normal agriculture soil and natural water conditions are short lived compounds with a median half life of 2.9 days. Under these conditions, the environmental exposure from 2,4-D esters and 2,4-D amine salts is expected to be minimal in both terrestrial and aquatic environments. Further analysis is required on reason(s) for 2,4-D BEE persistence in sediments from aquatic field studies. Additionally, the persistence of 2,4-D EHE on foliage and in leaf litter in registrant submitted forest field dissipation studies requires additional investigation. No field dissipation data (terrestrial, forest, or aquatic) have been submitted for the amine salts, 2,4-D IPA, 2,4-D TIPA, and 2,4-D DEA, or for the esters 2,4-D BEE (aquatic field dissipation data is available for this chemical form) and 2,4-D IPE to determine their persistence under field conditions.

Nontarget Terrestrial Species Risk

Birds

- No definitive endpoint was available from avian acute dietary studies, so that risk was not evaluated using an acute dietary endpoint. However comparison with the lowest dietary LC_{50} of >5620 mg ae/kg-diet would result in no acute level of concern (LOC) exceedances.
- For most small birds and some medium birds, when data from oral gavage studies were compared to predicted maximum exposures, there are exceedances of acute LOCs for all use sites except potatoes and citrus
- There are also exceedances of acute restricted use and endangered species LOCs for medium and large birds feeding on short grass, tall grass, and broadleaf forage/small insects at all use sites except potatoes and citrus.
- In general, when oral gavage data is compared with predicted mean exposures, RQs will be lower, but will still result in multiple restricted use and endangered species LOC exceedances, and a few acute LOC exceedances at the higher use rate sites such as non-cropland and asparagus.
- For chronic exposure of birds to non-granular spray, exceedances of chronic LOCs occurred for forage on shortgrass for use of 2,4-D on asparagus, cranberries, forestry, and non-cropland.
- Consideration of the non-granular spray average application rates results in reduction of chronic risk, but not to below LOCs.

Mammals

- Acute LOCs for mammals feeding on plants and insects were exceeded for use of

non-granular formulations for all uses assessed for small and medium size mammals except in potatoes and citrus. There were no exceedances for granivores.

- Banded applications result in exceedances of acute LOCs at all use sites.
- Mammalian chronic RQs range from 0.05 to 200 and chronic LOCs were exceeded in all cases with the exception of potatoes and citrus (large insects, seeds).
- Consideration of average application rates results in EECs below the LOCs for non-granular, granular, or banded applications. However, consideration of average application rates for non-granular, granular and banded applications did not result in exposure below the chronic LOC.

Plants

- For nontarget terrestrial plants, the RQs resulting from granular broadcast applications range from 2.2 (single application) to 266 (multiple applications) for the acid and amine salts and from 2.0 to 1702 for the esters.
- According to the 2,4-D Master Label the only use sites which allow applications of granular formulations are the non-crop land sites, turf, and cranberries.
- Acute LOCs for both non endangered and endangered terrestrial plants were exceeded for non-granular and granular uses at many use sites. Consideration of average application rates did not result in exposure below LOCs.

Nontarget Aquatic Species Risk

Terrestrial applications

- There were no acute or chronic LOC exceedances for aquatic organisms through use of 2,4-D acid and amine salts due to runoff/drift from use on terrestrial sites.
- There were no acute LOC exceedances for aquatic organisms due to drift-only of 2,4-D esters to water bodies from use on terrestrial sites.
- There were no acute LOC exceedances for aquatic organisms due to the runoff/drift of 2,4-D esters to water bodies from use on terrestrial sites.
- For non-target, aquatic plants, the runoff/drift of 2,4-D acid and amine salts from use on terrestrial crops results in an exceedance of the aquatic vascular plant endangered species LOCs for use of 2,4-D acid and amine salts on pasture and apples.
- Consideration of average application rates results in EECs below the endangered species LOC.
- For non-target aquatic plants, there are no LOC exceedances for either the scenario incorporating exposure resulting from the drift of the ester forms to aquatic water bodies or from the runoff of the ester forms to water bodies from use on terrestrial sites.

Aquatic weed applications

- Use of 2,4-D acid and amine salts in aquatic weed control through direct subsurface application to water bodies results in an exceedance of the restricted use and endangered species LOCs for freshwater invertebrates. There are no chronic LOC exceedances for this use.
- Use of 2,4-D BEE in weed control through direct subsurface application to water bodies results in exceedances of the acute risk LOC for freshwater fish and invertebrates and chronic risk LOC for freshwater and estuarine fish and freshwater invertebrates when compared on an acid equivalent basis.
- Additional characterization of the potential risk associated with the direct application of 2,4-D for aquatic weed control was completed by back-calculating the target concentration needed to reduce EECs below LOCs. This indicates that for all 2,4-D chemical forms target concentration reduction of up to 10-fold still exceed all LOCs for aquatic organisms.
- The scenario of direct application to water for aquatic weed control for 2,4-D acid and amine salts indicates an acute and endangered species LOC exceedances for aquatic vascular and acute LOC exceedances for non-vascular plants.
- Use of 2,4-D BEE (the only ester registered for aquatic weed control) for direct application to water for weed control results in exceedances of all LOCs for vascular and an acute LOC exceedance for non-vascular plants.
- For all 2,4-D chemical forms, target concentration reduction of up to 100-fold still exceed all LOCs for aquatic plants.

Rice paddy application

- Use of 2,4-D acid and amine salts in rice paddies results in exceedances of the acute endangered species LOCs for freshwater invertebrates.
- The rice model used to predict these EECs is a screening level model which predicts concentration in tailwater at the point of release from the paddy. It is anticipated that once released, the concentration will be reduced and subsequently is expected to decrease away from the point of release.
- Consideration of average application rates results in EECs below the endangered species LOC.
- Use of 2,4-D acid and amine salts in rice paddies result in exceedances of the acute and endangered species LOCs for aquatic vascular plants. Consideration of average application rates results in EECs below the endangered species LOCs.

Endangered Species

- Overall, RQs exceed the Agency's levels of concern for endangered and threatened

freshwater fish and invertebrates, estuarine invertebrates, birds, mammals, aquatic vascular plants, and terrestrial non-target plants at many sites. There are currently no listed endangered estuarine invertebrates or non-vascular aquatic plants.

Summary of Pending Data

The following data will be required as confirmatory information in the reregistration eligibility decision for 2,4-D:

Toxicology Data Needs

- Developmental neurotoxicity study, a subchronic inhalation toxicity study, and a repeat 2-generation reproduction study [using the new protocol] addressing concerns for endocrine disruption [thyroid and immunotoxicity measures] are recommended to be conducted on 2,4-D.

Product and Residue Chemistry Data Needs

- Grape processing, wheat hay field trials, and limited irrigated crop studies (sugar beet roots and tops and strawberries) are recommended to support tolerance establishment/reassessment associated with the use patterns currently supported by Task Force II.

Environmental Fate Data Needs

The environmental fate database is essentially complete. However several studies have been classified as supplemental. The following studies will assist in fully evaluating the potential risks associated with 2,4-D:

- Additional data on the behavior of 2,4-D BEE under acidic to neutral aquatic conditions in a water/sediment system will aid in fully evaluating the aquatic use of 2,4-D BEE.
- A laboratory volatility study for 2,4-D IPE is necessary to assess the volatility of this ester.
- Terrestrial field dissipation studies (164-1) were required in 1995 for 2,4-D IPA, 2,4-D TIPA, and 2,4-D DEA but have not been submitted. These studies will aid in fully assessing the behavior of these chemical forms under actual use conditions.
- EFED believes a terrestrial field dissipation study for 2,4-D BEE will aid in fully assessing the behavior of this chemical form under actual use conditions.

- 2,4-D IPE is currently registered only as a growth inhibitor and therefore EFED does not believe a terrestrial field dissipation study is needed for this chemical form.
- Aquatic field dissipation studies (164-2) in a rice use scenario for 2,4-D IPA, 2,4-D TIPA, and 2,4-D DEA will aid in fully assessing the behavior of these chemical forms under actual use conditions.
- Aquatic field dissipation studies (164-2) in an aquatic weed control scenario were required in 1995 for 2,4-D IPA, 2,4-D TIPA, and 2,4-D DEA but have not been submitted These studies will aid in fully assessing the behavior of these chemical forms under actual use conditions.
- Forest field dissipation studies (164-3) were required in 1995 for 2,4-D IPA, 2,4-D TIPA, and 2,4-D DEA but have not been submitted. These studies will aid in fully assessing the behavior of these chemical forms under actual use conditions.
- EFED believes a forest field dissipation study for 2,4-D BEE will aid in fully assessing the behavior of this chemical form under actual use conditions.
- 2,4-D IPE is not used in forestry applications and therefore a forest field dissipation study is not needed at this time.

Ecological Effects Data Needs

The ecological toxicity data base is fairly complete with the exception of the terrestrial plant testing on the typical end-use product (TEP). In addition to plant testing with TEP the following studies will assist in fully evaluating the potential risks associated with 2,4-D:

- Estuarine Fish - Since environmental fate data suggest that 2,4-D esters may persist under certain conditions and RQs associated with freshwater fish indicate potential risk to fish for 2,4-D BEE, further acute testing with 2,4-D BEE will aid in fully assessing the toxicity of this ester.
- Estuarine/marine invertebrates, acute - Since environmental fate data indicate that 2,4-D esters may persist under certain conditions and RQs associated with freshwater invertebrates indicate potential risk to aquatic invertebrates for 2,4-D BEE, further acute testing with 2,4-D BEE will aid in fully assessing the toxicity of this ester.
- Estuarine and Marine Invertebrate, Chronic - Since freshwater chronic risk quotients are exceeded for 2,4-D BEE (13.05), a chronic study will aid in fully assessing the risks associated with 2,4-D BEE for marine invertebrates.
- Sediment toxicity testing - Due to the persistence and high toxicity of the 2,4-D BEE granular formulation when used in a direct application to water a sediment toxicity test following EPA guidelines is requested on the granular formulation.
- Non-Target Terrestrial Plants - Currently, no studies following the EPA protocols are available for the 2,4-D sodium salt, and some data is missing or unavailable for

some of the other active ingredients. Current EFED policy requires testing of the TEP because these products sometimes include surfactants or adjuvants to increase the absorption to the foliage and may increase the toxicity of the product.