Chapter 4

Hazards and Hazardous Materials Impacts Assessment

4. Hazards and Hazardous Materials Impacts Assessment

This chapter analyzes the effects of the WHCP related to hazards and hazardous materials. The chapter is organized as follows:

A. Environmental Setting

B. Impact Analysis and Mitigation Measures.

The environmental setting describes existing conditions related to hazards and hazardous materials in the Delta. The impact analysis provides an assessment of the specific environmental impacts due to hazards and hazardous materials potentially resulting from program operations. The discussion utilizes findings from WHCP environmental monitoring and research projects, technical information from scientific literature, government reports, relevant information on public policies, and program experience. The impact assessment is based on technical and scientific information.

For each of the potential WHCP impacts related to hazards and hazardous materials we provide a description of the impact, analyze the impact, classify the impact level, and identify mitigation measures to reduce the impact level. For Impact H2: Treatment crew exposure, we provide a lengthy assessment of potential hazards and impacts related to worker exposure to 2,4-D and glyphosate. Because of the many uncertainties inherent in long-term human exposure to chemicals, this discussion is more detailed than many of the other impacts assessments.

The mitigation measures are specific actions that DBW will undertake to avoid, or minimize, potential environmental impacts. DBW has undergone, and will continue to undergo, consultation with various local, State, and federal agencies regarding impacts and mitigation measures. Proposed mitigation measures may be revised, and/or additional mitigation measures incorporated, as a result of this ongoing consultation with regulatory agencies.

A. Environmental Setting

There are numerous laws and regulations at the federal, State, and local levels that address hazardous materials. The most relevant federal law relating to the WHCP is the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA establishes jurisdiction over the distribution, sale, and use of pesticides. At the State level, the California Department of Pesticide Regulation (DPR) implements one of the most rigorous pesticide oversight programs in the country. DPR oversight includes product evaluation and registration, environmental monitoring, residue testing of fresh produce, and local use enforcement through the County Agricultural Commissioners.

There are two major State laws related to hazardous materials. The first law is the Hazardous Materials Release Response Plans and Inventory Act of 1985. This law requires businesses using hazardous materials to prepare a hazardous materials business plan. The second law is the Hazardous Waste Control Act, which creates the State's hazardous waste management program. The California program is more stringent than the federal Resource Conservation and Recovery Act (RCRA) that regulates hazardous waste.

1. Health Hazards

The Delta is a drinking water source for approximately 23 million Californians. If Delta projects compromise the quality of drinking water, more extensive treatment may be required. We discuss drinking water in Chapter 5, and water utility intake pumps in Chapter 6.

2. Hazardous Materials and Waste

Hazardous material and wastes are those substances that, because of their physical, chemical, or other characteristics, may pose a risk of endangering human health or safety or of endangering the environment (California Health and Safety Code Section 25260). In the Delta, hazardous waste sites associated with agricultural production activities include storage facilities and agricultural ponds or pits contaminated with fertilizers, herbicides, or insecticides.

Petroleum products and other materials may be present in the soil and groundwater near leaking underground storage tanks used to store these materials. Leaking or abandoned pesticide storage containers also may be present on farmland. Water from agricultural fields on which fertilizers and pesticides are applied may drain into ponds, and rinse water from crop duster tanks and other application equipment routinely is dumped into pits. Evaporation can increase chemical concentrations in pond water and cause chemicals to be deposited in underlying soil. Surface water percolation can pollute groundwater and expand the area of soil contamination.

Spills and leaking tanks or pipelines from industrial and commercial sites also can be sources of contaminants, such as petroleum hydrocarbons and polychlorinated biphenyls from old electrical transformers.

B. Impact Analysis and Mitigation Measures

For purposes of this analysis, we considered an impact related to hazards and hazardous materials to be significant and require mitigation if it would result in any of the following:

- Create a significant hazard to the public or the environment through the routine transport, use, or disposal of hazardous materials
- Create a significant hazard to the public or the environment through reasonably foreseeable upset and accident conditions involving the release of hazardous materials into the environment
- Emit hazardous emissions or handle acutely hazardous materials, substances, or wastes within one-quarter mile of an existing or proposed school
- Be located on a site which is included on a list of hazardous materials sites compiled pursuant to Government Code Section 65962.5
- For a project located within an airport land use plan, or where such a plan has not been adopted, within two miles of a public airport or public use airport, result in a safety hazard for people residing or working in the project area
- For a project within the vicinity of a private airstrip, result in a safety hazard for people residing or working in the project area

- Impair implementation of or physically interfere with an adopted emergency response plan or emergency evacuation plan
- Expose people or structures to a significant risk, injury, or death involving wildland fires.

Table 4-1, on the next page, provides a summary of the potential WHCP impacts for hazards and hazardous materials significance areas which could potentially be affected. Table 4-1 also explains those hazards and hazardous materials significance areas in which there will be no impacts or beneficial impacts.

Impact H1 – General public exposure: there is potential for the WHCP to create a significant hazard to the public through the routine transport, use, or disposal of WHCP herbicides

The general public could be exposed to WHCP herbicides through: consumption of drinking water contaminated with herbicides, consumption of fish or other aquatic organisms that have bioaccumulated WHCP herbicide residues, or swimming or water skiing in areas recently treated with WHCP herbicides.

We discuss the potential for drinking water contamination by WHCP herbicides in Chapter 5. The potential for WHCP herbicides to be present in concentrations in excess of USEPA Maximum Contaminant Levels (MCLs) of 70 ppb for 2,4-D, and 700 ppb for glyphosate, is extremely low. In addition, DBW will implement mitigation measures (including Mitigation Measure W1b, directed specifically at drinking water quality) to further reduce the potential for drinking water contamination by the WHCP.

We discuss the potential for WHCP herbicides to bioaccumulate in fish or other aquatic organisms in Chapter 3. Neither WHCP herbicide is expected to bioaccumulate in fish or aquatic species.

Potential exposure of the general public to WHCP chemicals through water recreation is unlikely. We discuss the toxicity of WHCP herbicides to humans under Impact H2, below. Herbicide exposure levels for the general public following WHCP treatments are orders of magnitude lower than potentially toxic herbicide levels.

WHCP treatments generally take place in heavily infested waterways, which are unsuitable for water recreation. It is unlikely that recreationists or nearby inhabitants would be close enough to WHCP treatments to come in contact with herbicides. Inhalation exposure basically applies to just applicators, not the general public (WDOE 2001). In addition, inhalation exposure for both glyphosate and 2,4-D are low. The vapor pressure of glyphosate is very low, and inhalation of spray droplets was found to be a minor route of glyphosate exposure (Acquavella et al. 2004). Exposure to glyphosate appeared to be very limited for those not in the immediate area of mixing, loading, or application activities (Acquavella et al. 2004 and 2005). Ibrahim et al. (1991) reported that studies of applicators showed that only 2 percent of the 2,4-D body burden was through respiratory exposures.

The Weedar® 64 label does not specify a waiting period for water recreation following aquatic weed control. Treated water should not be used for drinking water for three weeks, or until the 2,4-D level is no more than 0.1 ppm (100 ppb). WHCP monitoring results show 2,4-D levels significantly lower than 0.1 ppm, even one hour after treatment. The Aquamaster™ label states that there are no restrictions on the use of treated water for irrigation, recreation, or domestic purposes.

Table 4-1
Crosswalk of Hazards and Hazardous Materials Significance Criteria, Impacts, and Benefits of the WHCP

Significance Criteria and Impacts	Mitigation Measures	Unavoidable or Potentially Unavoidable Significant Impact	Avoidable Significant Impact	Less than Significant Impact	No Impact	Beneficial Impact
a) Create a significant hazard to the public or the environment through the routine transport, use, or disposal of hazardous materials?						
Impact H1: General public exposure	17			X		
Impact H2: Treatment crew exposure	3, 7, 18, 19, 20		X			
b) Create a significant hazard to the public or the environment through reasonably foreseeable upset and accident conditions involving the release of hazardous materials into the environment?						
Impact H3: Accidental spills	19		X			
c) Emit hazardous emissions or handle hazardous or acutely hazardous materials, substances, or waste within one-quarter mile of an existing or proposed school?					WHCP will not emit hazardous emissions or handle hazardous or acutely hazardous materials, substances, or waste within one-quarter mile of an existing or proposed school	
d) Be located on a site which is included on a list of hazardous materials sites compiled pursuant to Government Code Section 65962.5 and, as a result, would it create a significant hazard to the public or the environment?					WHCP will not be located on a site which is included on a list of hazardous materials sites compiled pursuant to Government Code Section 65962.5	
e) For a project located within an airport land use plan or, where such a plan has not been adopted, within two miles of a public airport or public use airport, would the project result in a safety hazard for people residing or working in the project area?					WHCP will not be located within an airport land use plan, or within two miles of a public airport or public use airport	
f) For a project within the vicinity of a private airstrip, would the project result in a safety hazard for people residing or working in the project area?					WHCP will not be located within the vicinity of a private airstrip or result in a safety hazard for people residing in or working in the project area	
g) Impair implementation of or physically interfere with an adopted emergency response plan or emergency evacuation plan?					WHCP will not impair implementation of or physically interfere with an adopted emergency response plan or emergency evacuation plan	Removal of water hyacinth could improve access to waterways used by emergency boats
h) Expose people or structures to a significant risk of loss, injury or death involving wildland fires, including where wildlands are adjacent to urbanized areas or where residences are intermixed with wildlands?					WHCP will not expose people or structures to wildland fires	

Based on existing research evidence, program operations, and monitoring results, WHCP herbicide treatments are not likely to result in adverse effects on the general public due to drinking water exposure, consumption of aquatic species that have bioaccumulated WHCP herbicides, or exposure to herbicides during recreation. **The potential for the WHCP to create a significant hazard to the public through routine transport, use, or disposal is expected to be less-than-significant.** No mitigation measures are required, however several of the mitigation measures that reduce the potential for herbicide exposure identified in Chapters 3 and 5 will further minimize the already low risk of hazard to the general public. In addition, DBW will implement the following Mitigation Measure to further reduce potential for public exposure to WHCP herbicides.

- **Mitigation Measure H1a** – Minimize public exposure to herbicide treated water.

  Prior to treatments, DBW will notify marina and dock owners regarding timing of treatments. WHCP treatments generally take place in heavily infested waterways, which are usually unsuitable for water recreation. If recreationists are present when treatment occurs, treatments crews will inform recreationists about the treatment, asking them to move to a different location, or move treatments to a different location.

Impact H2 – Treatment crew exposure: there is potential for the WCHP to create a significant hazard to treatment crews through the routine transport, use, or disposal of WHCP herbicides; and/or through heat exposure

The potential for the WHCP to create a significant hazard to treatment crews through the routine transport, use, or disposal of WHCP herbicides depends on the same two factors discussed for Biological Resources toxicity impacts: exposure and toxicity. However, in relation to humans, there are even greater uncertainties regarding exposure levels and short- and long-term toxicity of WHCP herbicides.

Pesticide workers, such as WHCP treatment crews, are exposed to higher levels of herbicides, and over longer time horizons, than the general public (Burns 2005). Some WHCP crew members have been with the program for over fifteen years. Each year, treatments take place as many as four days a week, over a six month period. This small group of individuals is uniquely exposed to WHCP herbicides over relatively long periods of time.

While animal toxicity studies can be used to assess the potential for human toxicity, particularly acute toxicity, it is much more difficult to determine whether there are long-term human impacts resulting from exposure to herbicides. Alavanja et al. (2004) noted that there are questions as to whether laboratory short-term toxicity studies of a single chemical are adequate to determine human exposure to a mix of chemicals over a lifetime, stating "neither animal testing alone or its interpretation in setting policy is sufficient to protect public health."

In reviewing the use of herbicides, the USEPA, World Health Organization (WHO), United States Forest Service (USFS), and other agencies evaluate the extensive scientific literature on each chemical, and identify exposure levels intended to ensure worker and public safety. These agencies reevaluate herbicide safety every few years as new studies are released. In the discussions below, we draw on recent agency analyses, as well as scientific literature on potential exposure levels and impacts of WHCP herbicides on humans.

In addition to potential hazards from herbicide exposure, WHCP treatment crews are potentially at risk due to heat exposure. Below, we assess the potential for herbicide exposure, short-term toxic impacts of herbicides, long-term chronic effects of herbicides to treatment crews, and heat exposure.

Scientific Terminology Related to Animal and Human Health Studies

Case-control epidemiological study – a study in human populations in which individuals with a specific diagnosis (e.g. non-Hodgkin lymphoma (NHL)) are identified and compared to similar controls in the population without the diagnosis. Typically these studies use questionnaires or telephone interviews to identify exposure and other characteristics of each group. Results are typically adjusted for other non-exposure factors related to the disease (e.g. smoking, age). The most commonly cited problem with case-control studies is recall bias on exposure information.

Cohort epidemiological study – a study of a group of people, a cohort, usually with a common characteristic, such as occupation. Subjects are evaluated over an extended period of time, comparing diseases among the cohort to diseases among the general population or subgroups within the cohort. Cohort studies also use questionnaires to determine exposure, but may also employ biomonitoring to measure exposure. Cohort studies may examine disease and exposure in the past (retrospective), or future (prospective). To prove linkages, cohort studies require a large number of participants, particularly if the disease being studied is rare.

Odds ratio (OR) – is a comparison of the odds of a condition existing among the exposure group, as compared to the odds of a condition existing among the control group. In pesticide epidemiological studies, it is often used to compare exposure to a pesticide among the case group (with the disease), to exposure to a pesticide among the control group (without the disease). The OR equation is:

$$\text{OR} = \frac{p_1/q_1}{p_2/q_2}$$

An OR of 1 means that there are equal odds of the exposure occurring among both groups. An OR of greater than one means that the group with the disease (the case group) had a greater chance of having been exposed than the control group. An OR of below one means that the case group had less chance of exposure than the control group. An OR of 2 means that the case group was twice as likely to be exposed to the pesticide as the control group. All figures are typically expressed with a 95 percent confidence interval (CI): for example, OR 1.3 (95 percent CI of 0.7 to 3.4). An OR is not considered statistically significant unless the lower bound CI is greater than one (although an OR with a lower bound of less than one may still be indicative of a need for further study or a potential risk). The following is an example OR: in one case-control study, 32 of 170 NHL patients (cases) treated seeds with fungicides, as compared to 105 of 948 controls. The example showed an elevated risk (almost double) of NHL among those that used fungicides, with an OR of 1.9 (Hoar 1986):

$$\text{Cases: } \frac{32}{170} = 0.19 \qquad \text{Controls: } \frac{105}{948} = 0.11$$

$$\text{OR} = \frac{p_1/q_1}{p_2/q_2} = \frac{\frac{0.19}{0.81}}{\frac{0.11}{0.89}} = 1.91$$

Risk ratio (RR) – or relative risk ratio, is a comparison of the disease rates among exposed and non-exposed groups over a specific time period. RR is typically used in cohort studies to compare the risk of a particular cancer or disease in the cohort, to the risk in a non-exposed population (often further adjusted for age, sex, etc.). Similar to the OR, a RR of one means that there is equal risk among the exposed and non-exposed groups, while a RR of greater than one means that there is a greater risk among the exposed group, and a RR of less than one means that there is less risk among the exposed group. RRs are also typically reported with a 95 percent confidence interval. For example, in a cohort study, 63 of 40,376 farmers exposed to glyphosate developed melanoma (0.16 percent), while 12 of 13,280 farmers not exposed to glyphosate developed melanoma (0.09 percent). The RR is equal to 0.16/0.09, or 1.8. This means there was an 80 percent increased risk of melanoma associated with glyphosate use (De Roos et al., 2005).

Standard Mortality Ratio (SMR) – is the ratio of observed deaths to expected deaths, for a particular disease. If there were one out of 2,500 (0.04 percent) melanoma deaths in the cohort being studied, and the expected deaths from melanoma was two per 100,000 (0.002 percent), the SMR would be equal to 0.04/0.002, or 20.

In vitro – experiments conducted in a controlled environment, outside of a living organism. In vitro experiments typically use cellular material, cell cultures, or tissue cultures.

In vivo – experiments conducted using whole living organisms. In vivo experiments include animal testing and clinical trials.

Reference Dose (RfD) – is the dose to humans, as determined by USEPA, at which there is a reasonable certainty of no harm. It is usually calculated by taking the lowest animal NOEL, and dividing by a safety factor of at least 100. The safety factor is determined by multiplying by 10 for each point of uncertainty. For example, a safety factor of 100 is based on a factor of 10 for sensitivity between species (assuming humans are more sensitive than animals), and a factor of 10 for sensitivity among species (for sensitive populations such as children). For 2,4-D, the safety factor is 1,000, as there is an third factor of 10 due to uncertainty in the database of studies. RfDs may be calculated for acute and chronic exposure. For chronic exposure, since the NOEL is based on lifetime exposure, the RfD represents the tolerable daily dose over a lifetime.

Hazard Quotient (HQ) – is calculated by dividing the exposure level by the RfD. An HQ of 1 or greater indicates a level for which there is concern related to long-term exposure. The higher the HQ, the greater the level of concern for the development of adverse health outcomes. An HQ of below 1 indicates that adverse health outcomes would not be expected.

Weight-of-evidence review (WOE) – is generally a qualitative review in which an individual or panel rates and assesses the scientific literature addressing a particular hypothesis, typically the relationship between a compound and a disease outcome (Krimsky 2005). A WOE considers all varieties of evidence and types of studies (in vivo, in vitro, epidemiological studies). Reviewers may give greater weight to certain types of studies or to studies based on statistical significance of results. Krimksy notes that WOEs often "use a process methodology that is low on transparency and high on subjectivity." However, it is often not possible or ethical to conduct human testing on toxic or potentially toxic agents. Thus, the WOE is an important tool particularly in cases of environmental exposure to chemicals, when no single study resolves issues related to exposure and causation.

Chlorphenoxy, Phenoxy, or Phenoxyacetic Acid Herbicides

The WHCP herbicide 2,4-D (2,4-dichlorophenoxyacetic acid), is one of a family of herbicides known as chlorphenoxy, phenoxy, or phenoxyacetic acid herbicides. Many of the studies discussed in this section included phenoxy herbicides as a group, not specifically 2,4-D. Phenoxy herbicides were developed in the 1940s, and have been used extensively worldwide since that time. The family name is based on the presence of chlorine, and phenoxyacetic acid. Two other herbicides in this group are MCPA (4-chloro-2-methylphenoxyacetic acid), and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid). The 50:50 combination of 2,4-D and 2,4,5-T, known as Agent Orange, was used in Vietnam as a defoliant. 2,4,5-T contains dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin) as an impurity. Dioxin is highly toxic to humans, and as a result 2,4,5-T was banned in the United States, and in most other countries, by 1985. There has been some concern about impurities in 2,4-D, although typically it is thought not to contain dioxins (USFS 2006). In addition, most studies used in 2,4-D risk assessments use technical grade 2,4-D, which would include any impurities that do exist in the herbicide (USFS 2006). There are multiple forms of 2,4-D, including acid, dimethylamine salt (the form used in the WHCP), and esters. Generally, these types of 2,4-D are thought to have similar toxicity in mammals.

Exposure to WHCP Herbicides

It is extremely difficult to measure exposure levels to pesticides in humans – either in pesticide applicators, their family members, or the general public. An estimated 25 million agricultural workers worldwide experienced unintentional pesticide exposure each year during the 1990s (Alavanja et al. 2004).

In many exposure studies, pesticide worker exposures are based on answers to written or telephone questionnaires about their historical use of various chemicals, and/or about current chemical use. When subjects are deceased, researchers must rely on family members to answer detailed questions about past chemical exposure. Recall bias can result in both overestimating and underestimating chemical exposure. In some cases, researchers adjust reported exposure levels using exposure algorithms (e.g. increasing exposure factors if the worker does not wear personal protective equipment (PPE)). Even if there was perfect recollection of chemicals used and worker safety practices, these studies cannot measure actual amounts of chemical absorbed or inhaled.

Researchers also conduct biomonitoring to identify actual body loads of chemicals in exposed workers. Barr et al. (2006) note that biomonitoring can provide a "rough estimate of internal dose", given assumptions about factors such as chemical uptake, metabolism, and steady-state excretion. Exposure to chemicals is usually in mg per kg body weight per day (mg/kg/day), or simply mg/kg body weight (mg/kg).

Biomonitoring includes measures of skin absorption, inhalation, and internal metrics. The amount of chemical absorbed by skin can be measured with patches, washing and wiping, and fluorescent tracers (Fenske 2005; Dosemeci et al. 2002). Inhalation is measured through personal air or air sampling (Fenske 2005). Internal chemical concentrations can be measured in urine, saliva, sweat, semen, and blood (Fenske 2005; Dosemeci et al. 2002).

Urine samples are another tool for measuring actual body load of chemicals that are excreted in urine. Urine samples must be adjusted for volume, depending on whether they are 24 hour samples, first void samples, or spot samples (Barr et al. 2006). A single spot urine sample measurement can provide information on whether exposure occurred, and some information on the magnitude of the exposure, but cannot provide information on total body load of the chemical. There are methods of extrapolating from single urine samples to total urine volume (and thus to determine total body load), for example using urine creatinine concentrations. The creatinine method introduces some uncertainty into the measurement, but is valuable in cases when it is not practical to obtain 24 hour urine samples.

We can estimate WHCP treatment crew exposure based on results of other studies that have evaluated pesticide applicator exposures in an agricultural or forestry setting. Exposure depends on characteristics of the chemical, conditions during application, and worker safety factors.

Numerous studies (Alavanja 2007; Hoar et al. 1986; Zahm and Blair 1992; Acquavella et al. 2004 and 2005; Mandel et al. 2005; Lavy et al. 1982) have shown that pesticide applicators that use PPE have lower risk and lower pesticide levels in blood or urine. In a talk to the North American Pesticide Applicator Certification and Safety Education Workshop in 2007, Dr. Michael Alavanja of the Agricultural Health Study, noted that proper glove use was the most influential item of PPE to mitigate chronic pesticide exposure (Alavanja 2007). Factors that increased exposure levels included fixing equipment during treatments, and more frequent mixing and loading of chemicals (Acquavella et al. 2004). In studies of urinary 2,4-D levels in applicators, predictors of herbicide levels included pesticide formulation, protective clothing and gear (especially gloves), handling practices, application equipment, personal hygiene, and type of spray nozzle used (Fenske 2005). Attitudes toward risk (as determined by questionnaires) played an important role in chronic exposure, as well (Alavanja 2007).

Exposure levels can also be influenced by outside factors and conditions. For example, USFS (2006) reported that several studies have found that sunscreen enhanced dermal absorption of 2,4-D. In addition, individuals that are pregnant, immune-compromised, malnourished, or have sickle-cell anemia, may be more sensitive to herbicides such as 2,4-D (USFS 2006).

WHCP treatment crews follow herbicide label requirements for PPE. This includes use of coveralls, chemical resistant gloves, safety goggles, and waterproof shoes. The DBW uses a laundry service to clean coveralls after a single day use. Herbicides are mixed using a feeder tube to draw chemical into the mixing tank, so that direct contact with the chemicals is not required. Potential exposure routes include dermal exposure when rinsing, or in the event that a feeder tube is broken. More likely exposure may occur through inhalation of drift in the event that the wind shifts during treatment. None of these exposure routes is likely, although they may occur.

2,4-D

Approximately 90 percent of WHCP treatments utilize 2,4-D. Thus, 2,4-D is of most concern as it relates to WHCP treatment crew exposure. Because it has been widely used, there are a number of studies in the literature on pesticide applicator exposure to 2,4-D. Chlorphenoxy herbicides are absorbed well from the gastrointestinal (GI) tract, less well from the lungs, and minimally from skin (Reigart and Roberts 1999).

Dermal exposure studies have found low dermal penetration of 2,4-D (WDOE 2001). One study found that approximately six percent of a dose was absorbed through the skin over a five day period. Other studies have found somewhat higher dermal absorption, ranging from seven percent to 14 percent (WDOE 2001).

Inhalation uptake of 2,4-D in humans has not been well studied, but rat studies found that 2,4-D was rapidly absorbed in lungs (Ibrahim et al. 1991). However, data from studies of applicators showed that respiratory sources only contributed two percent of total 2,4-D body burden (Ibrahim et al. 1991). In USEPA's 2005 review of 2,4-D, USEPA considered 2,4-D to be of low toxicity via acute inhalation exposure. USEPA also recommended that more inhalation studies be conducted to determine how rapidly the herbicide is absorbed via inhalation (USFS 2006). The half-life of 2,4-D in humans is 12 to 33 hours, thus most 2,4-D is excreted in urine within a few days.

Below, we summarize the results of several 2,4-D exposure studies. All studies focused on pesticide applicators, including farmers, forestry workers, or manufacturing workers.

- As part of the Farm Family Exposure Study, Mandel et al. (2005) examined 2,4-D levels in the urine of 34 farmers. Chemical levels were measured the day before treatment, the day of treatment, and for each of three days following treatment with 2,4-D. The geometric mean concentration of urinary 2,4-D was 64 ppb on the day of treatment, with a wide range of 2 ppb to 1,856 ppb. Skin contact and repairing equipment during treatment were associated with increased exposure. A relatively high 71 percent of applicators had detectable 2,4-D in their urine even before treatment, with a pre-treatment geometric mean of 4 ppb. This Farm Family Exposure Study also evaluated levels of glyphosate and chlorpyrifos after treatment with those herbicides. The study found higher urinary 2,4-D levels for farmers using 2,4-D, than corresponding urinary herbicide levels for farmers using glyphosate or chlorpyrifos
- Garry et al. (2001) evaluated 2,4-D urinary levels in forest pesticide applicators, by application method. Garry found that the highest 2,4-D levels were in forest pesticide applicators using back pack sprayers, closely followed by boom sprayers, then aerial application, skidders, and non-exposed controls, in that order. Garry found a ten-fold difference between the average urinary 2,4-D concentrations in back pack and boom sprayers (380.1 ppb) and the average urinary 2,4-D concentrations in aerial and skidder closed-cab applicators (33.2 ppb)
- Garry et al. (2001) also reported on a previous study that found workers employed in chlorophenoxy herbicide manufacture could have urinary 2,4-D levels over 1,000 ppb. This was significantly higher than most applicator studies, which typically found urinary 2,4-D levels in the range of 45 to 326 ppb
- Lavy et al. (1982) measured exposure to 2,4-D during aerial application, using respiratory exposure, skin patches, and urine levels. Workers applied herbicide at the rate of 4 lbs acid equivalent per acre, the same rate as the WHCP. Lavy tested 2,4-D levels in 18 forestry workers, including pilots, mechanics, mixers, supervisors, and flagmen. Using respiratory monitoring, only one worker (a mixer) had measurable 2,4-D levels, at 0.03 μg/kg. Using skin patches, most workers had non-detectable levels, and those with detectable levels ranged from 0.0005 mg/kg to 0.0409 mg/kg. Thirteen workers had detectable 2,4-D in urine, with 2,4-D levels in urine ranging from 0.00044 mg/kg to 0.0337 mg/kg (0.44 ppb to 33.7 ppb). Urine was measured over eight days total
- A Canadian study of 2,4-D acid residues in semen of 97 Ontario farmers that had recently used the herbicide found that 50 percent of samples had detectable 2,4-D residues of greater than 5ppb (Arbuckle et al. 1999)
- Studies of occupational exposure to 2,4-D reported in Ibrahim et al. (1991) found the highest daily exposure dose of 3.4 to 4.9 mg/day (equivalent to 0.05 to 0.07 mg/kg/day for a 70 kg person) for individuals using back pack sprayers on right-of-ways. The next highest exposures were found in farmers driving tractors (0.48 mg/day), and hand and tank commercial lawn sprayers (0.29 mg/day). There was a wide range of 2,4-D exposures in helicopter and airplane applicators, from 0.005 to 1.04 mg/day

Table 4-2
Pesticide Applicator Exposure Estimates for 2,4-D

Type of Application	Exposure in mg/kg/lb a.e.	Exposure in mg/kg/day	Exposure in mg/day	Source
1. Back pack sprayer		0.05 to 0.07*	3.4 to 4.9	Ibrahim et al. 1991
2. Boom spray from tractor		0.007*	0.48	Ibrahim et al. 1991
3. Broadcast ground spray	0.0002 (0.00001 to 0.0009)	0.02 (0.0007 to 0.15)	1.4* (0.05 to 10.5)	USFS 2006
4. Airboat handgun	0.0009 (0.0004 to 0.002)			USFS 2006
5. Calculated WHCP Crew (July to September 2007)	0.0009 (0.0004 to 0.002) based on USFS 2006	0.008 (0.003 to 0.017)	0.56* (0.21 to 1.19)	Calculated using 8.6 lb a.e. per crew

* Calculated based on 70 kg person (154 pounds).

- USFS (2006) exposure assessments for workers for 2,4-D were approximately 0.02 mg/kg/day for broadcast ground spray workers. The upper exposure range for broadcast ground spray workers was 0.15 mg/kg/day, with a lower exposure range of 0.0007 mg/kg/day. Among the USFS worker categories, broadcast ground spray worker exposures are most similar to WHCP treatment crews, in terms of likely exposure. However, USFS assumptions include treatment of a significantly higher acreage than the WCHP boat treatments, at 66 acres to 168 acres per day. This difference means that USFS total daily work exposure estimates are much higher than for WHCP treatment areas that treat approximately two to three acres per day.

Table 4-2, above, summarizes worker exposure studies most similar to WHCP treatment exposures. USFS (2006) developed a model to determine worker exposure levels based on Forest Service practices and treatment methods (boom spray or broadcast ground spray application, direct foliar application, and aerial application).

USFS (2006) estimated average 2,4-D exposure for a boom spray worker was 0.0002 mg/kg per lb of active ingredient (a.e.) handled per day, with a range of 0.00001 to 0.0009 mg/kg/lb a.e.

USFS (2006) also reported on a study of four workers applying liquid formulation 2,4-D by airboat handguns. For airboat applicators, USFS found exposure rates estimated at 0.0009 mg/kg/lb a.e. handled, with a range of 0.0004 to 0.002 mg/kg/lb a.e.. Airboat exposures were slightly higher than the ground-based boom spray, which might take place from an enclosed cab. Although only four workers were monitored, we utilized this study to estimate exposure for WHCP treatment crews.

We estimated WHCP treatment crew exposure using USFS exposure metrics. The highest potential WHCP treatment exposure to 2,4-D occurs during the months of July through September. During these three months in 2007, the six WHCP treatment crews each applied, on average, approximately 8.6 pounds a.e. 2,4-D per day, four days per week. Using the USFS airboat exposure estimates, WHCP treatment crews were exposed to 0.008 mg/kg/day (with a range of 0.003 to 0.017 mg/kg/day). Assuming an average 70 kg weight (154 pounds), the exposure per crew member was approximately 0.56 mg/day (with a range of 0.21 to 1.19 mg/day).

Glyphosate

In 2007, the WHCP utilized glyphosate on only 14 percent of the total acres treated for water hyacinth. Thus, exposure to glyphosate is significantly lower than exposure to 2,4-D.

Glyphosate is poorly absorbed through the skin (USFS 2003). Lavy et al. (1992) found that even though forestry sprayers had significant dermal exposure to glyphosate, biomonitoring results indicated no absorption of glyphosate. Dermal studies have shown absorption of less than 2 percent glyphosate (Acquavella et al., 2004). In addition, the vapor pressure of glyphosate is very low, and inhalation of spray droplets was found to be a minor route of glyphosate exposure (Acquavella et al., 2004).

While glyphosate exposure has not been as heavily studied as 2,4-D, there are still a large number of studies evaluating potential exposure to glyphosate among pesticide applicators.

- In the Farm Family Exposure Study, Acquavella et al. (2004 and 2005) examined urinary glyphosate levels in 48 farmers just prior to glyphosate treatment, the day of treatment, and three days following. The geometric mean concentration of glyphosate in farmers was 3 ppb, with a maximum of 233 ppb, and a minimum below the limit of detection (LOD) of 1ppb. Farmers that didn't use rubber gloves had a higher geometric mean (10 ppb for those without gloves, versus 2 ppb for those with gloves). Only 50 percent of farmers that did wear gloves had urinary glyphosate values above the LOD, while 86 percent of those that didn't wear gloves had levels above the LOD. Based on urinary levels, Acquavella calculated the maximum systemic dose was 0.004 mg/kg, and the geometric mean systemic dose was 0.001 mg/kg. Generally, glyphosate exposure was low, as 40 percent of farmers didn't have detectable urinary levels on the day of application. In this Family Farm Exposure Study, urinary glyphosate levels were lower than the other two herbicides monitored, 2,4-D and chlorpyrifos
- Acquavella et al. (2004) reported that a study of forest workers found the highest urinary levels at 14 ppb glyphosate. This same forest worker study estimated a maximum systemic dose of 0.006 mg/kg
- USFS (2003) worker exposure estimates are 0.026 mg/kg/day glyphosate, with a range of 0.0009 to 0.16 mg/kg/day for direct ground spray. Broadcast ground spray, with a boom, has slightly higher exposure estimates, of 0.045 mg/kg/day, with a range of 0.001 to 0.3 mg/kg/day. Similar to the USFS estimates for 2,4-D, the broadcast ground spray figures are likely closest to the potential exposure for WHCP treatment crews. However, these USFS estimates are similar to the USFS estimates for 2,4-D (USFS 2006), in that they assume that crews treat approximately 100 acres per day
- Solomon et al. (2005) reported on other studies with glyphosate worker exposure estimates, with a peak estimated glyphosate exposure at 0.056 mg/kg, and chronic exposure of 0.0085 mg/kg/day based on an 8 hour day and 5 day work week. Among farmers, the greatest estimated systemic dose was 0.004 mg/kg.

Table 4-3, on the next page, summarizes estimates of glyphosate exposure levels among pesticide applicators. USFS (2003) developed a model to determine worker exposure levels based on Forest Service practices and treatment methods (boom spray or broadcast ground spray application, direct foliar application, and aerial application).

USFS glyphosate estimates for broadcast ground spray with a boom were based on a figure of 0.0002 mg/kg/lb a.e. applied, with a range of 0.00001 to 0.0009 mg/kg/lb a.e. (USFS 2003). To estimate potential WHCP treatment crew exposure to glyphosate, we use an estimate of 12 pounds a.e. per day for ten days of glyphosate treatment in the first two weeks of October 2007. This was the highest

Table 4-3
Pesticide Applicator Exposure Estimates for Glyphosate

Type of Application	Exposure in mg/kg/lb a.e.	Exposure in mg/kg/day	Exposure in mg/day	Source
1. Tractor with boom spray		0.001 (max 0.004)	0.07* (max 0.28)	Acquavella et al. 2004
2. Forestry workers (method not specified)		0.006	0.42*	Acquavella et al. 2004
3. Direct ground spray		0.026 (0.0009 to 0.16)	1.82* (0.063 to 11.2)	USFS 2003
4. Broadcast ground spray (boom)	0.0002 (0.00001 to 0.0009)	0.045 (0.001 to 0.3)	3.15* (0.07 to 21)	USFS 2003
5. Agricultural workers		0.0085 to 0.056	0.6* to 3.92	Solomon et al. 2005
6. Calculated WHCP Crew (October 2007)	0.0002 (0.00001 to 0.0009) based on USFS 2003	0.0024 (0.0012 to 0.0108)	0.168* (0.084 to 0.756)	Calculated using 12 lb a.e. per crew

* Calculated based on 70 kg person (154 pounds).

application period for glyphosate during the 2007 treatment period. Even during October 2007, only three crews were using glyphosate. Based on USFS estimates, glyphosate exposure to treatment crews during this time period was 0.0024 mg/kg/day, with a range of 0.0012 to 0.0108 mg/kg/day. For a 70 kg person, this is equivalent to glyphosate exposure of 0.168 mg/day, with a range of 0.084 to 0.756 mg/day.

Short-Term or Acute Toxicity of WHCP Herbicides to Humans

Acute toxicity of pesticides in humans is generally extrapolated from several different types of sources: acute toxicity studies in laboratory mammals, biomonitoring of exposed workers, and intentional or accidental human poisoning cases. It is highly unlikely that WHCP activities would result in acute toxicity to WHCP treatment crews. The levels of either herbicide required to induce acute toxicity are several orders of magnitude higher than any potential exposure, even in the unlikely event of an accident. The discussion on short-term toxicity of these herbicides is provided below for background.

2,4-D Short-Term and Acute Toxicity

2,4-D is considered moderately toxic (Ibrahim 1991). The MSDS warns that 2,4-D is corrosive, and causes irreversible eye damage (Nufarm 2006). Existing respiratory and skin problems may also be aggravated by exposure (Nufarm 2006). In 1996, phenoxy herbicides were listed ninth among pesticides causing symptomatic illnesses (acute toxicity), with 453 total cases (63 children less than six years, and 387 cases age six and older), based on data from National Poison Control Centers (Reigart and Roberts 1999).

The reference, *Recognition and Management of Pesticide Poisonings* (Reigart and Roberts 1999) states that phenoxy herbicides are moderately irritating to skin, eyes, respiratory, and GI linings. In humans, ingestion of large amounts (accidental or suicidal) results in metabolic acidosis, electrocardiographic changes, myotonia (stiffness and in-coordination of muscles, including the inability to relax contracted muscle), muscle weakness, and myoglobinurea (presence of myoglobin, an oxygen-carrying muscle protein, in the urine). Several of these symptoms reflect injury to striated muscle. Clinical poisoning

cases also often result in hyperthermia (elevated body temperature).

Most fatal outcomes of phenoxy herbicide poisoning involve renal failure, acidosis, electrolyte imbalance, and resultant multiple organ failure. In patients with phenoxy herbicide poisoning, clinicians may see vomiting, diarrhea, headache, confusion, and bizarre or aggressive behavior, peculiar odor on breath, hyperventilation, muscle weakness, tachycardia, and hypotension. These changes are indicative of liver cell injury. Levels of 2,4-D exposure required to achieve these symptoms are high. Herbicide applicators with blood 2,4-D levels at, or below, one mg/l (ppm) to two mg/l may have no symptoms. Cases of 2,4-D poisoning in which the patient was unconscious reported blood levels from 80 mg/l to 1,000 mg/l 2,4-D (Reigart and Roberts 1999).

In large doses to experimental animals, phenoxy herbicides caused vomiting, diarrhea, anorexia, weight loss, ulcers of mouth and pharynx, myotonia, and toxic injury to liver, kidneys, and the central nervous system (Reigart and Roberts 1999). Mammal 2,4-D LD50 values ranged from 100 mg/kg for dogs to 1,000 mg/kg for guinea pigs (Ibrahim et al. 1991). The 2,4-D salt form had LD 50s ranging from 375 mg/kg for mice to 2,000 mg/kg for rats. Most LD 50s, except dogs, range from 300 to 1,000 mg/kg (Ibrahim et al. 1991).

The Washington State Department of Ecology (WDOE 2001) reviewed a range of 2,4-D toxicity studies. The WDOE review found that neurotoxicity studies of 2,4-D were negative, and recent studies did not provide evidence that 2,4-D was immunotoxic. These studies did conclude that when 2,4-D was administered to test animals in high doses, there were histopathological changes in many organ systems, but primarily the kidney and liver. Researchers believe that once kidney function is compromised, mammals cannot excrete 2,4-D effectively. This, in turn, increases the amount of chemical in the animal's system, causing more harmful impacts. In a study examining the thymus and spleen of rats following exposure to 2,4-D at a dose of one-half the LD50 (228 mg/kg), Kaioumova et al. (2001) concluded that 2,4-D appeared to be causing hemolytic activity, destroying the vascular integrity of thymus and causing cell depletion in white pulp of spleen.

In a study of forest pesticide applicators following one-time application of 2,4-D, Garry et al. (2001) examined chromosome aberrations, reproductive hormone levels, and polymerase chain reaction-based rearrangements (indicative of altered genomic stability) . The study compared these biomarkers to urinary 2,4-D levels in 24 applicators and 15 controls. Applicators using hand-held backpack sprayers had the highest 2,4-D urinary levels, averaging 453.6 ppb. Among applicators, researchers found serum luteinizing hormone(LH) levels increased, correlated with urinary 2,4-D levels. They did not see similar changes in follicle stimulating hormone or testosterone. Chronically increased LH can lead to significant increases in testosterone, but the increases seen in this study were not of immediate clinical concern, and Garry was not sure what impact these reproductive hormone disruptions might have on male reproductive potential. Applicators with higher 2,4-D exposure levels (measured by urine 2,4-D) had rearrangements of DNA, but follow-up ten months later suggested that these DNA changes were reversible and temporary. The 2,4-D levels were not correlated with chromosome aberration frequencies. Garry et al.'s previous laboratory work had suggested that most phenoxy herbicides were not genotoxic at the chromosome level, and that these herbicides (or their adjuvants) may have had some endocrine disrupting activity. Garry et al. determined that "acute, high-level exposure to 2,4-D as measured by urinary concentration with or without adjuvant use, is not associated with detectable chromosome damage in G-banded lymphocytes."

Glyphosate Short-Term and Acute Toxicity

Glyphosate is not hazardous according to the federal Occupational Safety and Health Administration (OSHA) Hazard Communications Standard (Monsanto 2005). In humans, glyphosate can be irritating to eyes, skin, and upper respiratory tract (Reigart and Roberts 1999).

Among California occupational illnesses likely due to pesticides between 1991 and 1995, glyphosate was listed seventh, with nine systemic cases and 94 topical cases (skin, eye, or respiratory), for 103 total glyphosate illnesses reported (Reigart and Roberts 1999).

USFS (2003) reported on toxic impacts of glyphosate exposure to humans, creating a dose-response scale. Many of these exposures resulted from intentional ingestion of glyphosate. At calculated doses of 184 mg/kg in humans, there were "no apparent effects" from glyphosate. At the higher dose of 427 mg/kg, there was "mild poisoning," including transient signs and symptoms in oral mucosa or GI tract. More than double this dose (1,044 mg/kg) resulted in "moderate poisoning," with GI irritation, transient hepatic or renal damage, decreased blood pressure, and pulmonary dysfunction. Finally, "severe poisoning," which was fatal, occurred in patients that had consumed about 1,282 mg/kg. The lowest dose of 184 mg/kg would require drinking just under one ounce of Aquamaster™, while the highest dose of 1,282 mg/kg would require drinking just over ¾ of a cup of Aquamaster™. Neither of these scenarios is realistic within the framework of the WHCP.

Acute toxicity levels for glyphosate in animal studies were similarly high, with LD50 values ranging from 2,000 to 6,000 mg/kg in a number of test animals (USFS 2003). Toxic effects of glyphosate are thought to be related to uncoupling of oxidative phosphorylation (the process that converts energy from nutrients to storage in high-energy phosphate bonds). This uncoupling results in loss of energy and eventual death, and inhibition of hepatic mixed function oxidases (enzymes that are involved in metabolism of a wide range of endogenous compounds and xenobiotics) (USFS 2003).

Chronic Effects of WHCP Herbicides to Humans

Long-term or chronic toxicity effects include cancer, reproductive toxicity, teratogenicity, endocrine disruption, immunotoxicity, genotoxicty, mutagenicity, mental and emotional functioning, and damage to specific tissues or organs. Long-term toxicity can be evaluated through in vivo and in vitro studies, as well as epidemiological studies. Many epidemiological studies focus on farmers and pesticide applicators, as they tend to be exposed to pesticides over a long time period. WHCP treatment crew exposure may be similar to both of these groups.

Very little is understood about the health effects of low doses of pesticide exposure over a long time period. For every published study indicating that a particular pesticide or group of pesticides causes cancer, there is another published study indicating that the same pesticide does not cause cancer. It is extremely difficult to prove causation, and to sort out confounding factors such as exposure to multiple chemicals. In this section, we will first discuss general findings and issues related to the effects of long-term pesticide exposure, followed by discussion of studies specific to 2,4-D[1] and glyphosate.

General long-term effects

There have been hundreds of studies examining the effects of chronic pesticide exposure over the last several decades. Many of these studies have

[1] Many of the studies of long-term impacts of 2,4-D are for phenoxy herbicides more generally, or for each of several phenoxy herbicides.

shown a wide range of impacts including solid tumors, haematological cancers, genotoxic effects, mental and emotional functioning, and reproductive effects (Cohen 2007). For cancers, one of the key factors to consider is the link between exposure and biological plausibility. Is there a mechanism by which the pesticide in question could have induced the resulting cancer?

There is controversy as to whether chronic exposure to pesticides (as a broad category) is neurotoxic, and epidemiological studies linking pesticides and human cancers are inconsistent (Alavanja et al. 2004).

Generally, insecticide exposure is thought to be linked to neurotoxic effects, with less linkage for herbicides (Kamel et al. 2005). One study found that increased neurological symptoms were linked to increased cumulative lifetime days of exposure, particularly for organophosphate and organochlorine insecticides (although all classes of insecticides showed increases). Hong et al. (2006) examined neurobehavioral performance in organic farmers and pesticide using farmers in Korea. Hong found, based on a variety of tests, no apparent effect on either the peripheral or central nervous system in the pesticide users.

In one study, that did not identify specific herbicides and adjuvants, Burroughs et al. (1999) examined hormone levels in the bloodstream of agricultural workers in four groups: (1) controls; (2) herbicide only applicators; (3) herbicide and adjuvant applicators; and (4) applicators using herbicides, fumigants, and insecticides. Only the herbicide only applicator group showed a significant difference in hormone levels from controls. The herbicides evaluated included, but were not limited to, phenoxy herbicides. Burroughs also looked at in vitro impacts on genotoxicity, and found that all four adjuvants had a dose-response curve showing genotoxicity, but only one (unspecified) herbicide showed genotoxicity.

López et al. (2007) examined antioxidant enzymes in 81 pesticide applicators during the spraying season. López saw decreased enzyme activity during the spraying season, but was not sure if this decreased enzyme activity was related to adverse health effects. This study did not look at specific pesticides.

Blair and Zahm (1995) reviewed studies of agricultural exposure and cancer in the literature. Farmers were generally healthier than the overall population, but they appeared to have increased risks of some cancers, including: leukemia, NHL, multiple myeloma, soft-tissue sarcoma (STS), and cancers of the skin, lip, stomach, brain, and prostate. Blair and Zahm noted that the number of excess cancers were not large, but were noticeable because farmers were otherwise healthier than normal, and because the tumors were not smoking related. The study did not identify any established etiological factors for the cancers, but stated that some were associated with immune system deficiencies (Blair and Zahm 1995). The study also noted the need to evaluate exposures to materials other than pesticides, such as fuels, oils, engine exhausts, organic solvents, dusts, and microbes.

One of the largest efforts aimed at identifying long-term health impacts related to pesticides is the Agricultural Health Study (AHS). AHS is a prospective cohort study of over 89,000 farmers, pesticide applicators and spouses in Iowa and North Carolina. The study is sponsored by the National Institute of Health (NIH) and USEPA. The goal of the AHS is to "investigate the effects of environmental, occupational, dietary, and genetic factors on the health of the agricultural population."

Through the AHS, government scientists and collaborating academics and others have conducted a number of studies using the entire AHS cohort, as well as specific sub-groups. Data gathering has been ongoing. When they entered the program between 1993 and 1997, farmers

and spouses completed questionnaires, and many completed a second, more detailed, take-home questionnaire. A Phase 2 follow-up took place between 1999 and 2003 (this included buccal (mouth) cell collection, a computer assisted telephone interview, and a mailed dietary questionnaire). A Phase 3 follow up began in 2005 (this included a third interview, DNA analysis, and questionnaire validation).

Overall, farmers and spouses in the AHS have a lower than expected risk of cancer than the general public in North Carolina and Iowa. However, for some specific cancers, such as prostate cancer, AHS participants have higher risks. While some cancers among AHS participants may be related to specific pesticides, there is not enough data yet to make any such conclusions (Alavanja et al. 2005). The AHS has shown that individuals that applied pesticides more than 400 days in their lifetimes had a higher risk of Parkinson's disease (as self-reported), compared with those that applied pesticides for fewer days. Again, there was not enough data to link the occurrence of Parkinson's to certain pesticides, although it is still being studied (Kamel 2006).

In the AHS examination of prostate cancer among male pesticide applicators, researchers evaluated over 55,000 applicators and 45 pesticides. They also controlled for known and suspected risk factors. While the overall risk of prostate cancer among AHS participants was higher, there were no elevated risks for prostate cancer among farmers exposed to glyphosate-family and phenoxy herbicides (Alavanja et al. 2003).

A more recent study of AHS pesticide applicators (Belseler et al. 2008) found a link between depression and pesticide exposure, suggesting that both acute high-intensity and cumulative pesticide exposure may contribute to depression in pesticide applicators. Three percent of the study population of almost 18,000 applicators reported depression symptoms. The highest level of lifetime days of exposure (over 752 days) showed a statistically significant relationship to depression. When researchers examined depression by exposure to major pesticide groups, use of herbicides showed a strong association with diagnosed depression, with an odds ratio (OR) of 2.0. The 95 percent confidence interval (CI) was not statistically significant, ranging from 0.76 to 5.54. For insecticides, the OR was 1.96, with a statistically significant 95 percent CI of 1.29 to 3.27. Belseler et al., (2008) concluded that "results suggest that pesticide exposure may contribute to depression in farmer applicators and the importance of minimizing pesticide exposures. Future work on neurological effects of pesticide exposure should include measures of affective disorders, including depression and anxiety."

These examples illustrate the significant uncertainty as it relates to pesticide exposure and long-term health impacts in humans. The uncertainties are even greater when one considers specific pesticides, such as 2,4-D and glyphosate. While researchers attempt to adjust their results for exposure to multiple chemicals and other risk factors such as age and smoking, it is extremely difficult to draw specific conclusions about the long-term impacts of these herbicides.

2,4-D long-term effects

Worldwide, 2,4-D is one of the most widely used herbicides. The chemical has been extensively studied, and while there are many conflicting studies, regulatory agencies at all levels consistently state that when used as specified, 2,4-D does not pose human health risks.

The Industry Task Force II on 2,4-D Research Data (Task Force), an industry funded research organization, provided a news release in 2006 summarizing several assessments on 2,4-D. The

Task Force cited a 2004 USEPA review that concluded "there is no additional evidence that would implicate 2,4-D as a cause of cancer." USEPA stated that none of the recently reviewed epidemiological studies "definitely linked human cancer causes to 2,4-D." The release also cited assessments by WHO, and Health Canada's Pest Management Regulatory Agency that did not identify health risks from 2,4-D. The Task Force identified 23 separate regulatory decisions or expert panel reviews, dating from 1987 to 2005, that have concluded that 2,4-D does not present an unacceptable risk when used according to product instructions (Industry Task Force II 2006).

Despite these assessments on the safety of 2,4-D, there continues to be conflicting results and studies on various potential long-term impacts of 2,4-D. This uncertainty is evident in the California Department of Pesticide Regulation (DPR) assessment of 2,4-D. In the DPR Summary of Toxicology Data for 2,4-D (which was last updated in August 2006), there were five impact categories for 2,4-D that were identified as having a "possible adverse effect" – chronic toxicity rat, chronic toxicity dog, oncogenicity mouse, reproduction rat, and DNA damage.

One of the most controversial issues surrounding the use of 2,4-D is the potential link between 2,4-D and NHL. We discuss studies on NHL separately, following discussions of other potential long-term impacts of 2,4-D and glyphosate.

Another set of controversy surrounds the potential genotoxicity, mutagenicity, neurotoxicity, immunotoxicity, endocrine disruption, and/or reproductive effects of 2,4-D. There have been numerous published studies, at all levels, with both positive and negative effects. There are two primary potential reasons cited for the differing results: 1) the use of different grades of 2,4-D (reagent versus commercial), and 2) the differing endpoints of these various studies, in terms of media and timing (Tuschl and Schwab 2003; Madrigal-Bujaidar et al. 2001).

These studies demonstrate significant conflicting evidence surrounding the long-term effects of 2,4-D. Many studies that show negative effects of 2,4-D utilize relatively high doses, and/or cellular culture systems that do not include normal in vivo protective mechanisms. However, given the difficulty in measuring impacts of any chemical or combination of chemical and environmental factors, particularly over the long-term, it seems prudent to minimize worker exposure to 2,4-D to the greatest extent possible.

Further reflecting the controversy surrounding potential impacts of 2,4-D, in December 2008, the USEPA published an announcement seeking comments on a National Resources Defense Council (NRDC) petition to revoke all tolerances and cancel all registrations for 2,4-D (Federal Register 2008). One of the comments surrounding the USEPA evaluation of pesticides, including 2,4-D, is that the USEPA relied on studies submitted by industry for the registration process, and not on the open scientific literature. The comment period for the NRDC petition ended February 23, 2009; however, there was no published time frame for further USEPA action on 2,4-D. As of June 2009, the USEPA had received over 500 comments on the petition. In May 2009, the NRDC asked the USEPA to first address residential uses of 2,4-D, rather than agricultural uses.

Researchers have used a wide range of methodologies to examine long-term impacts of herbicides such as 2,4-D. The studies summarized below include in vitro, in vivo, and epidemiological studies, and several weight-of-evidence reviews. While a comprehensive summary of all studies on 2,4-D is beyond the scope of this Draft PEIR, we include a sampling of summaries of these studies to illustrate the issues related to potential impacts of long-term exposure to 2,4-D.

In vitro analyses of 2,4-D include a wide variety of tests using various forms of 2,4-D in cellular cultures. Media evaluated include yeast, salmonella (Ames test), human erythrocytes, hamster ovary cells, germ cells, and others. There are published studies that illustrate various cytotoxic, genotoxic, mutagenic, or other effects, and studies that do not. As noted above, the use of different grades of 2,4-D, and different media and endpoints, may explain some of the variability. Several of these studies illustrate mechanisms of action for 2,4-D, some of which may be negated by in vivo protective mechanisms. For example, oxidation resulting from 2,4-D may be reduced by natural anti-oxidant systems in the cell. Most in vitro studies involve exposing the cellular medium to varying concentrations of 2,4-D for a set time period, then evaluating various end points. Most exposure levels are well above those likely to result from WHCP treatments, typically in the ppm, rather than ppb, range.

- Morelmans et al. (1984) found no mutagenic activity in four Salmonella strains tested with 2,4-D and other phenoxy herbicides at 2,4-D levels of 10 and 100 μg/test plate
- Mustonen et al. (1986) found that pure 2,4-D did not increase chromosome aberrations in human peripheral lymphocyte cultures, but a commercial 2,4-D formulation did increase chromosome breaks and aberrations at concentrations ranging from 54 to 217 ppm
- Holland et al. (2002) found increased effects with commercial as compared to pure 2,4-D; however genotoxic and cell cycle effects were relatively minimal for both. At 1 ppm commercial 2,4-D, they found a marginally significant increase in replicative index, a metric that indicates changes in cell cycle kinetics. There was also an increase in micronucleus formation at higher concentrations (217 ppm). Micronucleus formation is a marker of genotoxicity
- Gollapudi et al. (1999) and Charles et al. (1999) found no evidence of genotoxicity in cultures of rat lymphocytes and Chinese hamster ovary cells exposed to 2,4-D
- Venkov et al. (2000) found increases in gene conversions, reverse mutations, and moderate cytotoxic effects that were time and dose related in yeast cells exposed to 1,736 ppm 2,4-D
- Maire et al. (2007) found that 2.5 and 5 ppm 2,4-D induced cell transformation, but not apoptosis (cell death) in Syrian hamster cells
- Lin and Garry (2000) examined commercial and reagent grade 2,4-D in MCF-7, a breast cancer cell line. They found that higher doses of the commercial grade induced cell proliferation at the higher doses. As there were no impacts with the reagent grade, they hypothesized that additives in the commercial product were responsible for the estrogen-like receptor mediated proliferation. They also noted that because internal cell mechanisms would likely dampen the estrogen-like effects, one would not necessarily see these results in a clinical trial
- Tuschl and Schwab (2003) examined changes in cell cycle progression in the human hepatoma cell line (HepG2 cells) following exposure to 868 ppm, 1,736 ppm, or 3,472 ppm 2,4-D. The highest dose resulted in apoptosis due to reduced mitochondrial membrane potential. The lower two doses resulted in changes in cell cycle progression
- Bukowska et al. (2008) demonstrated that 2,4-D induced oxidation in human erythrocytes through the formation of free radicals. Effects, seen at doses ranging from 9.8 ppm to 542 ppm, ranged from changes in mitochondria potential, capase (an enzyme) dependent reactions, and apoptosis. 2,4-D induced oxidation in a time and dose dependent manner, although it did not result in denaturation of haemoglobin

- Gonzalez et al. (2005) found that 2,4-D at 6 ppm and 10 ppm increased sister chromatid exchange (sister chromatid exchange is an indicator of genotoxicity), reduced mitotic index (a measure of cell proliferation), and increased DNA damage in Chinese hamster ovary cells
- Bharadwaj et al. (2005) found indications of cell proliferation, changes in gene expression, and cytotoxicity at 22 ppm, 217 ppm, and 868 ppm 2,4-D in human hepatoma HepG2 cells
- Teixeira et al. (2004) evaluated the level of free radicals in yeast cells exposed to 2,4-D, and found that 2,4-D induced the formation of free radicals and stimulated the activity of anti-oxidant enzymes in a dose and time dependent fashion. Concentrations of 2,4-D ranged from 98 ppm to 141 ppm
- Moliner et al. (2002) exposed cerebellar granule cells to 217 ppm and 434 ppm 2,4-D. They found reduced cell viability, increases in apoptotic cells, increased capase 3 activation, and reduced cytochrome c. They concluded that 2,4-D induced apoptosis by direct effect on mitochondria
- Zeljezic et al. (2004) examined the genotoxic effect of 2,4-D on human lymphocytes at relatively low levels (86 ppb and 868 ppb). Both concentrations resulted in an increase in chromatid and chromosome breaks, increased number of micronuclei, and increased number of nuclear buds, all signs of genotoxicity
- Soloneski et al. (2007) examined the genotoxic effects of 10 ppm to 100 ppm 2,4-D on human lymphocytes with, and without, erythrocytes present. They found the highest dose to be cytotoxic, with delays in cell cycle progression and reduced mitotic index at the lower doses. They also noted that with erythrocytes present, none of the concentrations induced sister chromatid exchange, indicating that erythrocytes in the culture system modulated the DNA and cellular damage inflicted by 2,4-D
- Bukowska (2003) identified changes in anti-oxidant enzyme systems in human erythrocytes exposed to 250 ppm and 500 ppm, indicative of the oxidative effect of 2,4-D. In a later study, Bokowska et al. (2006) examined acetylcholinesterase activity in human erythrocytes, showing reduced enzyme activity at 500 ppm and 1,000 ppm 2,4-D, again indicative of oxidative activity of 2,4-D
- Bongiovanni et al. (2007) evaluated the oxidative stress produced by 2,4-D in rat cerebellar granule cells. They measured oxidation properties in cells exposed to 217 ppm 2,4-D, with and without the presence of melatonin, a known anti-oxidant. Melatonin countered most of the oxidative changes induced by 2,4-D, supporting the efficacy of melatonin as a neuroprotector
- Mi et al. (2007) examined the oxidative impacts of 2,4-D with, and without, another anti-oxidant, quercetin. Without quercetin, 50 ppm 2,4-D resulted in a number of oxidative impacts on chicken embryo spermatogonial cells, including: condensed nuclei, vacuolated cytoplasm, reduced cell viability, increased lactate dehydrodgenase, increased malondialdehyde, reduced glutathione, and reduced superoxide dismutase. Exposure to 2,4-D with quercetin reduced impacts to the same levels as controls, indicating that dietary quercetin may attenuate the negative effects of environmental toxicants.

In vivo analyses of 2,4-D exposure in laboratory animals typically involve feeding animal subjects 2,4-D at various doses, specified as mg/kg/day. Most laboratory study doses are well above potential worker exposure levels.

- Ibrahim et al., (1991) note that the dog subchronic NOEL is 10 mg/kg/day and rat chronic NOEL is 30 mg/kg/day. There was a NOEL for reproductive effects in rats of 10 mg/kg/day. This study found decreased birth weight in offspring even without apparent maternal toxicity

- de la Rosa et al. (2004) examined the impact of the herbicides propanil and 2,4-D in combination, and separately, on thymus weight (i.e. immune system impacts) in an in vivo experiment in mice. While the combination of the two herbicides did reduce thymus weight, propanil and 2,4-D alone did not
- USFS (2006) reported that a LOEL in canines of only 3 to 3.75 mg/kg/day (dogs are more sensitive to 2,4-D because they cannot excrete organic acids), and a LOEL in rodents of 75 to 100 mg/kg/day. At these doses, impacts included decreased body weight and food consumption, and adverse effects in the liver and kidney
- Charles and others conducted a number of studies for the 2,4-D Industry Task Force on chronic and subchronic effects of 2,4-D. Charles et al. (1996a) found reduced weight gain and other effects at up to 7.5 mg/kg/day in subchronic and chronic tests in dogs, but did not identify any immunotoxic or oncogenic impacts. In another 1996 study (Charles et al. 1996b) of 2,4-D chronic toxicity in rats and mice, the researchers identified impacts such as reduced weight gain, opthamalic impacts, and hematological impacts at higher doses, but no oncogenicity. Mattsson et al. (1997) identified mild, transient locomotor effects from high-level (250 mg/kg) acute exposure to 2,4-D, and retinal degeneration from high-level chronic exposure in female rats. They identified a NOEL for acute neurotoxicity of 15 mg/kg/day, and for chronic neurotoxicity of 75 mg/kg/day. In 2001, Charles et al. conducted developmental toxicity studies of 2,4-D in rats and rabbits, and concluded that no adverse fetal effects were noted at dose levels that did not also produce evidence of maternal toxicity, or exceed renal clearance of 2,4-D
- A group of scientists at the School of Biochemical and Pharmaceutical Sciences at the National University of Rosario in Argentina has investigated the impacts of 2,4-D since the mid-1990s. Many studies involved feeding pregnant and/or nursing rats doses of approximately 70/mg/kg/day (below the NOEL) to 100 mg/kg/day, and evaluating effects on both rat pups and mothers. In numerous published articles, the group has identified: reversible and irreversible behavioral alternations in pups (Bortolozzi et al. 1999); reduced body weight and central nervous system myelin deficits in rat pups (Duffard et al. 1996); neuron cell changes in rat pups (Brusco et al. 1997); transfer of 2,4-D from exposed dams to neonates (Stürz et al. 2000); changes in neurotransmitter receptors and brain weight in rat pups (Bortolozzi et al. 2004; Garcia et al. 2004); increases in 2,4-D milk residues as compared to maternal doses, reduced milk lipid content, changes in milk proteins and fatty acids, and impaired rat pup nutrition (Stürtz 2005); evidence of oxidative stress in brains of neonates exposed to 2,4-D in milk (Ferri et al. 2007); and disruptions in material behavior and neurotransmitter levels in exposed dams (Stürtz et al. 2008)
- Rawlings et al. (1998) found reductions in thryoxine levels, as compared to controls, in ewes receiving 10 mg/kg 2,4-D three times per week for 36 days. There were no overt signs of toxicity, including no effect on body weight. There were no reductions in other measured hormones, including leutenizing hormone (LH), insulin, estradiol, or cortisol
- Linnainmaa (1984) examined sister chromatid exchange frequency in the blood lymphocytes of rats and hamsters exposed one time to 100 mg/kg 2,4-D, and found no differences between treated and controlled rodents
- Mustonen et al. (1986) found no changes in cell cycle kinetics or chromosomal aberrations in the lymphocytes of workers exposed to 2,4-D. All workers did have measurable levels of 2,4-D in urine
- Lee et al. (2001) evaluated immune function in offspring of rats fed 8.5 mg/kg, 37 mg/kg, or 370 mg/kg 2,4-D during gestation. They found "subtle immune alterations" in offspring of the highest treatment group

- Chernoff et al. (1990) fed pregnant rats 2,4-D at the LD50 level, and four lower doses. They identified a number of effects, including reduced maternal weight, increased supernumary ribs in pups, and reduced thymus weight in pups
- After 12 and 24 hours, Venkov et al. (2000) found increases in chromosome aberrations and reduced mitotic index in mice intraperitoneally administered 3 to 5 mg/kg 2,4-D. They hypothesized that the cytotoxicity and mutagenicity were induced by the presence of chlorine atoms at positions 2 and/or 4 in the benzene ring of 2,4-D
- Madrigal-Bujaidar et al. (2001) found that 2,4-D induced moderate increases in sister chromatid exchange in both somatic and germ cells of mice exposed to a 50 to 200 mg/kg oral dose of 2,4-D
- Several studies suggested that 2,4-D adversely affects reproductive organs, particularly testes. Rats had lower testicular and ovarian weights at a dose of 75 mg/kg/day. Dogs had similar impacts at doses of 3 mg/kg/day. Impacts in both rats and dogs included lower testicular weights, inactive prostates, and deficient sperm production (USFS 2006).

Epidemiological studies of pesticide applicators and workers exposed to 2,4-D have examined a number of potential impacts (additional studies examining linkages between 2,4-D and NHL are described further below). Many of these studies identify areas of potential concern related to 2,4-D exposure, however it is nearly impossible to link chronic exposure to 2,4-D, with certainty, to any diseases.

- Swan et al. (2003) examined semen quality in relation to pesticide levels in blood for healthy men in Missouri and Minnesota to test whether reduced semen quality found in Missouri was linked to higher exposure to pesticides. Swan found strong odds ratios linking lower sperm quality to exposure to the pesticides alachlor, atrazine, and diazinon. They found "borderline with small and somewhat inconsistent associations" for 2,4-D and metolachlor. A small study in Argentina showed decreased sperm concentration and morphology related to high urinary levels of 2,4-D
- Faustini et al. (1996) examined blood levels of various immunological factors in ten farmers prior to exposure, within one to 12 days of exposure, and 50 to 70 days after exposure to 2,4-D and MCPA . They found immunosuppressive effects during the one to 12 days of exposure period, however most of the effects were short-term, and were no longer in evidence by 50 to 70 days after exposure
- Figgs et al. (2000) compared urinary and blood levels of 2,4-D in exposed workers, replicative index, micronuclei, and lymphocyte immunophenotypes in exposed workers. They found increased replicative index scores, indicative of stimulated cell growth, but no changes in lymphocyte immunophenotypes or micronuclei. Figgs et al concluded that there was no evidence of human chromosome damage at urinary levels of 12 to 1,285 ppb 2,4-D, and no support for genotoxicity of 2,4-D
- Holland et al. (2002) found that the lymphocyte replicative index, but not the mitotic index, was affected in applicators exposed solely to 2,4-D during a three-month period
- In a very general article, Buranatrevedh and Roy (2001) identified 2,4-D as endocrine disrupting, citing a 1988 study by Bond of chemical workers
- Burns (2005) (of Dow Chemical) reviewed several studies of pesticide applicators and manufacturers and cancer. Burns noted that while there are hundreds of such studies, few have focused on a single pesticide or class of pesticide, and that "limitations in sample size, exposure assessment, and the small number of studies make causal inference difficult." Burns noted that several studies of phenoxy herbicides, including 2,4-D, have found no increased risk of cancer. Other studies have shown an association between some of the lymphopoietic cancers and the use of

phenoxy herbicides. Some, but not all, case-control studies have shown an association between 2,4-D and NHL. Some studies examining exposure to herbicides in general have identified higher risk of NHL (for small farms), and for multiple myeloma. One meta-analysis of studies of farmers identified increased risk of NHL, but provided no details on exposures

- There is some indication that there is a potential link between 2,4-D exposure (in DOW workers) and ALS (amyotrophic lateral sclerosis) (Burns et al. 2001). There were only three cohort members in the study with ALS, which makes it difficult to draw conclusions. At least one researcher Freedman (2001) noted that this potential linkage warrants serious attention in future studies.

There have been a number of comprehensive weight-of-evidence reviews of 2,4-D conducted by scientists. In addition, regulatory agencies have conducted risk assessments that considered potential impacts of 2,4-D on workers. These evaluations identified several relevant conclusions.

- In 1992, Munro et al. conducted a comprehensive integrated review and evaluation of the scientific evidence relating to the safety of 2,4-D. All authors were from private research groups in Canada and Washington DC. Munro integrated data from worker exposure studies, whole animal studies, metabolic studies, and epidemiological studies
- Munro (1992) summarized that case-control studies linking 2,4-D with cancers were inconclusive, and that epidemiological studies, "provide, at best, only weak evidence of an association between 2,4-D and the risk of cancer"
- Munro (1992) also identified one of the most commonly cited criticisms of the potential link between 2,4-D and cancer, that the chemical structure of the herbicide, and animal studies, do not support that 2,4-D would be a carcinogen
- Munro (1992) further cited a large body of negative studies on genotoxicity of 2,4-D. These negative genotoxicity studies, together with the negative metabolic studies "clearly indicates that 2,4-D is highly unlikely to be a genotoxicity carcinogen." Munro also reviewed and found no evidence for adverse effects on immune system, endocrine system, neurotoxic effects, and reproductive effects (except at high acute toxic doses). Finally, Munro noted that historical exposure to 2,4-D was higher than current exposures, due to label changes and increased safety precautions that have been implemented
- In a weight-of-evidence analysis conducted by 12 scientists (and funded by the Industry Task Force II on 2,4-D), Ibrahim et al. (1991) evaluated the research (through 1989) on 2,4-D impacts. The panel reviewed published data, considered all evidence, and made weight-of-evidence judgments. The diverse panelists were not expected to all agree, and tried to capture their differences in the article. On mutagenicity, they found that: "although it has been one of the most rigorously tested compounds, the available evidence on the mutagenicity of 2,4-D and its related products is equivocal to negative. Evidence indicates it does not exhibit the gene-damaging potential of a classic mutagen." In vitro tests have shown both positive and negative mutagenicity results
- Ibrahim et al.'s (1991) analysis of carcinogen bioassays only considered those conducted after 1986, when procedures were refined. They summarized two two-year studies conducted in 1986 and 1987. One study on rats found a significant increase in brain tumors at the highest dose of 45 mg/kg/day 2,4-D, and two tumors in the second highest dose, 15 mg/kg/day. A similar study repeated on mice, did not find effects. The panel concluded, "considered together, these two animal studies do not provide impressive evidence that exposure to 2,4-D causes cancer in animals. Based on results from the rat study, the workshop participants

concluded that there was weak evidence supporting an excess of brain cancer occurrence in the male Fischer 344 rats receiving the highest dose"

- Ibrahim et al. (1991) also examined the cohort studies of 2,4-D and concluded, "in summary, the cohort studies provide little evidence to suggest that 2,4-D exposure increases the risk for more common types of cancers in humans." They only evaluated three of the six cohort studies that had been completed at the time, because the other three studies had small cohorts or low statistical power
- In Ibrahim (1991), the workshop participants did not find strong evidence between the exposure of 2,4-D and any other type of cancer, besides NHL, and were also not convinced that there was a cause-effect relationship between 2,4-D and cancer. Eleven of 13 participants said that it was "possible" that 2,4-D could cause cancer in humans, with one thinking the possibility was pretty strong, and five thinking that it was pretty weak. Two participants thought that it was unlikely that 2,4-D causes cancer in humans. Several panelist said that there was barely enough evidence to support any conclusions regarding carcinogenicity of 2,4-D
- WDOE (2001) summarize that 2,4-D is not considered to be a teratogen or reproductive hazard if administered below maternally toxic doses. This evaluation noted that there have been conflicting results on mutagenicity studies, but that an USEPA panel concluded, "2,4-D does not pose a mutagenic hazard and there is no concern for mutagenicity at this time." Animal carcinogenicity studies have not been positive. WDOE noted that epidemiological studies of 2,4-D exposed workers have been "controversial", and that studies haven't definitively demonstrated an association between 2,4-D and NHL or other cancer
- In 2002, Garabrant and Philbert conducted a review of human toxicity and cancer risks related to 2,4-D. This review, conducted for the Industry Task Force II on 2,4-D Research, focused on studies conducted between 1995 and 2001. Garabrant and Philbert focused their review on animal and epidemiological studies. They noted that "it is clear from the large amount of data available that 2,4-D, its salts, and esters are not teratogenic in mice, rats, or rabbits unless the ability of the dam to excrete the chemical is exceeded" (p.236). They also noted that it is unlikely that 2,4-D has any neurotoxic potential at doses below those that result in systemic toxicity. While Garabrant and Philbert discussed results of some in vitro studies, none of the three studies that they identified had positive results. The review concludes that despite several in vitro and in vivo studies, there is no experimental evidence that under physiologic conditions, 2,4-D causes DNA damage or is immunotoxic
- Garabrant and Philbert (2002) also summarized a large number of epidemiological studies. They noted many of the study weaknesses that had been previously identified, such as limited exposure data. The review did not find any compelling evidence among the case-control and cohort studies that 2,4-D was linked to soft tissue sarcoma, non-Hodgkin lymphoma, or Hodgkin lymphoma
- As part of the 2005 pesticide reregistration process, USEPA made a number of conclusions about 2,4-D, including that it had: low acute toxicity based on dermal, oral, and inhalation exposures; was a severe eye irritant; a Group D, non-classifiable carcinogen, based on the fact that it was not mutagenic, but that there were cytogenic effects (USEPA 2005). In the USEPA's reregistration approval of 2,4-D, they requested that a number of additional studies be completed to address areas of uncertainty related to 2,4-D's impacts. These included: a subchronic (28 day) inhalation study, a repeat two-generation reproduction study to address concerns related to endocrine disruption, and a developmental neurotoxicity study. USEPA noted that the endocrine disruption study should address concerns related to thyroid effects, immunotoxicity, and a more thorough assessment of the gonads and reproductive/developmental endpoints (USEPA 2005)

Table 4-4
Toxicity and Exposure Standards for 2,4-D and Glyphosate, Compared to Potential WHCP Exposure

Exposure Standard	2,4-D	Glyphosate
1. USEPA Chronic NOEL	5 mg/kg/day	175 mg/kg/day
2. USEPA Safety Factor	1,000	100
3. USEPA Chronic RfD	0.005 mg/kg/day	2 mg/kg/day
4. USEPA Acute NOEL	25 mg/kg/day (females) 67 mg/kg/day (general pop.)	175 mg/kg/day
5. USEPA Acute RfD	0.025 mg/kg/day (females) 0.067 mg/kg/day (general pop.)	2 mg/kg/day
6. WHO ADI	0 to 0.01 mg/kg/day	0.3 mg/kg/day
7. USFS HQ	16 to 30	0.2
8. WHCP Estimated Exposure	0.008 mg/kg/day (0.003 to 0.017)	0.0024 mg/kg/day (0.0012 to 0.0108)
9. WHCP Estimated HQ	1.6 (0.6 to 3.4)	0.0012 (0.0006 to 0.0054)

- In their risk analysis, USFS (2006) noted that 2,4-D is toxic to the immune system in recent studies, especially in combination with other herbicides. The toxicity mechanism is through cell membrane disruption and cellular metabolic processes. The herbicide was found to result in genetically programmed cellular death (apoptosis). Toxic effects started at the cellular membrane. In disrupting cellular metabolism, researchers hypothesized that because 2,4-D is similar to acetic acid, it forms analogues of the enzyme acetyl-Co-A, which is involved in glucose metabolism, and production of cholesterol, steroid hormones, and acetylcholine. By forming these analogues, 2,4-D disrupts these processes. 2,4-D may also cause apoptosis by directly damaging mitochondria, which initiates apoptosis in human lymphocytes.

The USEPA and other agencies determine pesticide levels that are considered safe for both long-term and short-term exposure. These agencies also make determinations about the carcinogenicity of various chemicals. Below (for 2,4-D), and in **Table 4-4,** above, we summarize current metrics for 2,4-D, and relevant figures for the WHCP, based on the exposure estimates in Table 4-2.

- USEPA maintains that 2,4-D is a Class D carcinogen, which is "not classified as to human carcinogenicity". The International Agency for Registration of Carcinogens (IARC) classifies 2,4-D as 2B, "possible carcinogen to humans". The World Health Organization (WHO) does not regard 2,4-D as genotoxic or carcinogenic (USFS 2006)
- USEPA uses a chronic NOEL of 5 mg/kg/day in rats, and a safety factor of 1,000 to calculate the chronic exposure RfD for 2,4-D of 0.005 mg/kg/day. The safety factor of 1,000 is based on safety factors of 10 each for sensitivity between species, sensitivity within species, and uncertainty in the database of study results. That is, the RfD is 1,000 times lower than the chronic NOEL, providing three orders of magnitude protection compared to the animal study NOEL. This RfD means that USEPA considers a daily lifetime exposure of 0.005 mg/kg/day to be safe (0.35 mg/day for a 70 kg person). This chronic RfD value is relevant for determining the potential risk of 2,4-D exposure to WHCP treatment crews
- USEPA uses two different acute NOEL values to determine acute RfDs. The lower acute NOEL of 25 mg/kg/day is for

females of reproductive age, while the higher 67 mg/kg/day is for the general population. These NOELs are based on animal acute toxicity studies. The acute RfD values are 1,000 times lower, at 0.025 mg/kg/day, and 0.067 mg/kg/day, for reproductive age females and the general population, respectively

- WHO identified an acceptable daily intake (ADI) for 2,4-D of between 0 and 0.01 mg/kg/day, based on a NOEL of 1 mg/kg/day
- USFS calculated a hazard quotient of 16 for backpack and aerial spray, and 30 for ground spray. These HQ values are based on the expected forest worker exposure, divided by the chronic RfD. An HQ greater than one indicates potential hazard. As a result, USFS (2006) noted that "based on upper bound hazard quotients, adverse health outcomes are possible for workers who could be exposed repeatedly over a longer-term period of exposure." The USFS exposure values, as summarized in Table 4-2, utilize significantly higher acreage per day treatment than the WHCP
- In Table 4-4, we calculate HQ values for estimated WHCP exposure, based on the exposure estimates for WHCP crews in Table 4-2, and the RfD of 0.005 mg/kg/day. Because WHCP crews are exposed to 2,4-D for only part of the year, these HQ values of over 1 may not be as potentially hazardous as it appears. The estimated WHCP HQ for 2,4-D is 1.6, with a range of 0.6 to 3.4. Thus, there is potential hazard to WHCP treatment crews from long-term exposure to 2,4-D.

Glyphosate long-term effects

Like 2,4-D, glyphosate is also a widely utilized and extensively studied herbicide. Similarly, glyphosate is generally considered safe for humans when used as specified. Another commonality is the conflicting results and ongoing controversy regarding the potential impacts of long-term exposure to glyphosate. In the DPR Summary of Toxicology Data for glyphosate (last updated November 1992), there were two impact categories identified as having a "possible adverse effect" – oncogenicity in mouse, and oncogenecity in rat. Monroy et al. (2005) stated that while glyphosate is considered to be of low health risk to humans, the occurrence of possible harmful side effects of glyphosate are not well documented and are controversial. Monroy notes that there have been studies that suggested glyphosate could alter various cellular processes in animals.

Below, we provide a summary of research on glyphosate to reflect the range of concerns that have been expressed. A full review of all such studies is beyond the scope of this Draft PEIR.

In recent years there have been a number of in vitro studies that have raised concerns related to glyphosate. Generally, in vitro studies provide a first-level assessment of potential toxicity and mechanisms, and can indicate a need for further analyses.

- Monroy et al. (2005) examined the toxicity and genotoxicity of glyphosate to normal human cells and human fibrosarcoma cells. Monroy noted a dose-dependent effect, with cytotoxic and genotoxic effects at concentrations of 4.0 to 6.5 millimolar (mM) (equivalent to 676 to 1,098 ppb). They concluded that the mechanism of action of glyphosate was not limited to plant cells
- Hokanson et al. (2007) noted that the general chronic toxicity of glyphosate has not been determined, but that it is considered to be an endocrine disrupter. Hokanson examined the possibility that glyphosate interrupts estrogen-related gene expression in an in vitro DNA microarray analysis. The study found that 680 of 1,550 genes were dysregulated by in vitro exposure to commercial glyphosate, but that many of the changes were minor. Hokanson concluded that "there remains an unclear pattern of very complex events following exposure of human cells to low

levels of glyphosate." They noted that exposure was complicated and potentially damaging to adult and fetal cells

- Glyphosate has generally been considered as harmless in normal usage, but Marc et al. (2004a) noted conflicting evidence. In a study of five glyphosate formulations (all with surfactant) on sea urchin embryos[2], Marc et al. identified a dose-dependent effect, proportional to the amount of glyphosate. Some of the five glyphosate products produced impacts at 1mM (169 ppb), while others required levels of 8 to 12 mM (1,352 to 2,028 ppb). Marc saw dysfunction and a delay in morphological changes in the cell cycle at 10 times higher doses, but saw no aberrant chromosome morphology. Marc concluded that the effect appeared to be common to a group of glyphosate products, but did not establish a direct link with development of cancer
- In a follow-up study of sea urchin embryo development using Roundup®, Marc et al. (2004b) found that glyphosate at 10mM (1,690 ppb) delayed occurrence of the first cell cycle by 30 minutes. The delay was caused by glyphosate interfering with DNA replication. Marc determined that the effect was due to glyphosate acting in synergy with surfactants. Glyphosate concentrations in soil or water are expected to be in the nanomolar range, and there is no indication that they would result in genotoxic effects at those lower levels, but formulated glyphosate is sprayed at a concentration of 40mM (6,760 ppb) – so applicators could potential inhale micro-droplets at these levels shown to be toxic to sea urchins.

In vivo animal studies have historically shown glyphosate chronic toxicity only at high levels. However, some recent studies indicate that there may be cellular responses to glyphosate at lower concentrations. Exposure levels, even in the chronic toxicity studies, are still several orders of magnitude higher than potential exposures to WHCP crews.

- Daruich et al. (2001) studied the activity of several enzymes in pregnant rats and fetuses exposed to glyphosate, and found a variety of functional abnormalities in enzyme activity
- Benedetti et al. (2004) examined glyphosate in rats, examining hepatic effects at three dose levels for 75 days. The doses were 4.87 mg/kg, 48.7 mg/kg, and 487 mg/kg. At even the lowest concentrations of glyphosate, Benedetti found leakage of hepatic intracellular enzymes, suggesting irreversible damage in hepatocytes
- Dallegrave et al. (2003) examined the teratogenic potential of Roundup in rats, at relatively high doses of 500 mg/kg, 750mg/kg, and 1,000 mg/kg. At the highest dose, there was 50 percent mortality of dams. Dallegrave found 33 percent of fetuses at the lowest 500 mg/kg dose had skeletal alternations.

There are fewer epidemiological studies of exposure to glyphosate than of 2,4-D. These studies generally show little, to no, chronic health concerns related to glyphosate.

- In introducing their study of cancer incidence among glyphosate-exposed pesticide applicators in the AHS, De Roos et al. (2005) noted that there have been conflicting results of genotoxicity studies related to glyphosate. Some studies have found no genotoxic activities of glyphosate, while others have found genotoxic effects. In the early 1990s, USEPA and WHO concluded that glyphosate was non-mutagenic, but some more recent case-control studies have suggested associations between glyphosate and NHL. This study by De Roos et al. examined risk of cancers among the AHS participants with exposure to glyphosate, adjusting for five other pesticides highly associated with glyphosate use. De Roos also adjusted for age, demographic, and lifestyle factors. Unlike many cohort studies, this study had large

[2] Sea urchin embryos have been found to be a good indicator of cell development in all species.

cohorts. There were 13,280 participants that had never been exposed to glyphosate, 15,911 participants with low exposure to glyphosate, and 24,465 participants with high exposure to glyphosate (as measured by questionnaires). The total number of cancers among all participants was 2,088. The researchers found no association between glyphosate exposure and increase in all cancers combined. Among specific cancers, they found an association between glyphosate exposure and melanoma, with a risk ratio of 1.8 (and a 95 percent CI of 1 to 3.4) when adjusted for age only. When adjusted for age and other lifestyle factors, the RR decreased to 1.6 (and a 95 percent CI of .8 to 1.6). The study did not observe any association between glyphosate and NHL. De Roos noted that the association between glyphosate and melanoma was based on a small number of cases. The association could result from spurious associations or chance, however some details were internally consistent indicating it was more than chance. The researchers were not sure of a causal pathway

- As reported by USFS (2003), the Ontario Farm Health Study, a retrospective cohort study of almost 2,000 farm couples, did not find linkages between glyphosate exposure and miscarriage, spontaneous abortion, or fecundity
- As part of their risk assessment in Columbia, Solomon et al. (2005) reported on a study evaluating whether glyphosate exposure was associated with adverse reproductive effects. They conducted a retrospective cohort study of 600 women of reproductive age in each of five regions in Columbia, comparing reproductive health to known pesticide use. They found no associations between fecundity and glyphosate spraying.

While not as extensively analyzed as 2,4-D, there have been a number of regulatory agency and third-party reviews of glyphosate.

- Williams et al. (2000) conducted a "current and comprehensive safety evaluation and risk assessment of glyphosate and Roundup®" (including POEA) for humans. They evaluated regulatory studies and published research reports. The review found low oral and dermal absorption of glyphosate, no bioaccumulation, and no significant glyphosate toxicity in acute, subchronic, and chronic studies. Williams did find that direct contact with glyphosate could result in ocular irritation, but noted that the potential for worker exposure was low
- Williams et al. (2000) applied a weight-of-evidence approach and standard evaluation criteria for genotoxicity data, and determined there was no convincing evidence for DNA damage in vitro or in vivo. They also did not find evidence of tumorigenic potential from multiple lifetime feeding studies in animals, and no effects indicative of reproductive, teratogenic, or endocrine disruption
- In their risk assessment of glyphosate, USFS (2003) reported that there were no neurotoxic, immune, or endocrine effects for glyphosate. USFS noted that there was potential for endocrine effects, because such effects have not been extensively evaluated
- USFS (2003) reported that a consistent sign of subchronic or chronic glyphosate toxicity is loss of body weight. Glyphosate likely acts as an uncoupler of oxidative phosphorylation, and may cause liver and kidney toxicity.
- Solomon et al. (2005) report that "overall, there is little epidemiological evidence to link glyphosate to any specific disease in humans." Their risk assessment of spraying coca and poppy with glyphosate in Columbia concluded that the risks to humans and human health were negligible.

USEPA and other agencies have determined glyphosate levels that are considered safe for both long-term and short-term exposure. These agencies also make determinations about the carcinogenicity of various chemicals. Below (for

glyphosate), and in Table 4-4, we summarize current metrics for glyphosate exposure, and relevant figures for the WHCP, based on the exposure estimates in Table 4-3.

- USEPA assigned glyphosate as Class E, "evidence of non-carcinogenicity in humans (no evidence in at least two adequate animal tests in different species or in both epidemiological and animal studies)". WHO has assigned a similar carcinogenicity classification for glyphosate
- USEPA utilizes a NOEL for both acute and chronic exposure to glyphosate of 175 mg/kg/day, based on a teratogenicity study in rabbits. The safety factor for glyphosate is 100, based on factors of 10 each for sensitivity between species and sensitivity within species. The acute and chronic RfD for glyphosate is 2 mg/kg/day, calculated by dividing 175 mg/kg/day by 100, and rounding up to 2
- Based on a regression analyses of human and animal toxicity data, the RfD is conservative, and appears to be very protective for both short- and long-term exposures (USFS 2003)
- WHO determined an ADI of 0.3 mg/kg/day, based on a NOEL of 31.5 mg/kg, and an uncertainty factor of 100. These values are lower than the corresponding USEPA figures, and are based on a life-time feeding study in rats
- USFS (2003) noted that for glyphosate, the highest calculated HQ for workers, 0.2, was still well below one, the level at which there is concern
- The estimated HQ for glyphosate exposure of WHCP treatment crews, even using conservative exposure assumptions, is only 0.0012. This HQ is three orders of magnitude below one, the level at which there is potential for concern. Thus, long-term exposure of WHCP treatment crews following program operational procedures, is considered safe.

Non-Hodgkin Lymphoma

Some of the most studied linkages between pesticides and cancer are those of non-Hodgkin lymphoma and 2,4-D, phenoxy herbicides, and/or pesticides in general. Much of this research followed a study by the Swedish researcher Hardell in 1981 that showed a link between phenoxy herbicides and NHL. As many of these studies described below illustrate, the evidence, in both directions, is conflicting. Below, we summarize several of the epidemiological studies on NHL and pesticides, including both 2,4-D and glyphosate.

- Hardell and Ericksson were among the first to report potential linkages between NHL and phenoxy herbicides. They have continued to evaluate linkages between NHL and pesticides since the early 1980s. Over the years, their studies have been both criticized and confirmed
- In one of several such studies, Hardell and Eriksson (1999) examined the risk of NHL among subjects exposed to herbicides in Sweden. This was a case-control study, with 400 cases and 700 controls. The team used questionnaires to estimate exposure. If the subject was deceased, a living relative answered the questionnaire (which was one of the (many) criticisms of their work). Hardell and Ericksson found an increased risk of NHL for herbicide exposure in general, with an OR of 1.6 (95 percent CI 1.0 to 2.5). For fungicide exposure the OR was 3.7 (95 percent CI 1.1 to 13), for phenoxyacetic acid exposure the OR was 1.5 (95 percent CI 0.9 to 2.4), and for MCPA exposure the OR was 2.7 (95 percent CI 1.0 to 6.9). This study did not consider 2,4-D exposure alone. Hardell and Ericksson also noted an increased risk of NHL with glyphosate exposure, with an OR of 2.3 (95 percent CI 0.4 to 13). The glyphosate risk was based on only four cases and three controls with exposure, and was not statistically significant. After conducting multivariate analyses, the odds ratios were somewhat reduced, and the researchers

determined that they could not make conclusions about linkages between NHL and specific chemicals

- The fact that Hardell and Ericksson raised concerns about glyphosate and NHL caused several individuals to criticize Hardell's 1999 study. Researchers from Monsanto, Harvard, and Yale commented that Hardell and Eriksson did not address the other evidence that glyphosate was not carcinogenic, that there were problems with the questionnaire approach to gathering exposure information, and that the conclusions were based on only a small number of cases (Acquavella and Farmer 1999; Cullen 1999; Adamie and Trichopoulos (no date)).
- In a recent study, Eriksson et al. (2008) again examined pesticides as a risk factor for NHL in Sweden, with 910 cases and 1,106 controls. Exposure was also based on questionnaires. General herbicide exposure resulted in an OR of 1.72 (95 percent CI 1.18 to 2.51), MCPA exposure resulted in an OR of 2.81 (95 percent CI 1.27 to 6.22), and glyphosate exposure had an OR of 2.02 (95 percent CI 1.16 to 4.40). Eriksson concluded that this study confirmed an association between phenoxyacetic acids and NHL, and strengthened understanding of association with glyphosate
- In their first of several studies, Hoar et al. (1986) examined agricultural herbicide use and risk of lymphoma and soft tissue sarcoma (STS) in a population based case-control study of Kansas residents. The researchers chose Kansas due to high use of 2,4-D. This study looked at NHL, Hodgkin's disease, and STS cases from 1976 to 1982. There were just fewer than 1,000 controls, matched to between 120 and 170 cases for each of the three cancers. The researchers conducted interviews of cases and controls to answer exposure and lifestyle questions. For the 130 farming subjects, Hoar also confirmed exposure by examining pesticide supplier records. Hoar analyzed the data using a variety of approaches. They found a six-fold increased risk of NHL among high intensity 2,4-D users, which was cause for concern. Among all 2,4-D users, there was an OR of 2.2 (95 percent CI 1.2 to 4.1). There was also higher risk of NHL if the subject didn't use protective equipment when applying pesticides. This study confirmed Hardell's work in Sweden, however Hoar noted that there were no carcinogenicity studies in animals, or evidence of immunosuppression by 2,4-D[3]
- In a follow up study Zahm (formerly Hoar) and Blair (1992) reviewed the possible role of pesticides in increases in NHL. They noted a link between NHL and 2,4-D in studies in Sweden, Kansas, Nebraska, and Canada. In addition, canine malignant lymphoma was associated with dog owner use of 2,4-D and commercial pesticide treatments. Zahm and Blair commented that several other chemicals were found to have possible links to NHL, including triazine herbicides, organophosphate insecticides, fumigants, and fungicides. Zahm and Blair reviewed 21 cohort studies of farmers that provided data on NHL and farming. These studies had risk ratios ranging from 0.6 to 2.6. Eleven of the studies reported higher risks of NHL with exposure to chemicals, but only three studies were statistically significant. Zahm and Blair commented that, "both the descriptive and analytical data tend to show excesses [of NHL], but are not impressive overall"
- De Roos et al. (2003) noted that "an increased rate of non-Hodgkin lymphoma (NHL) has been repeatedly observed among farmers, but identification of specific exposures that explain this observation has proven difficult." De Roos examined case-control data from the 1980s, with a total sample sized of over 3,500. The studies, based in the Midwest, looked at 47 pesticides simultaneously, and controlled

[3] Immunosuppression is linked to NHL.

for confounding factors. They found associations with several pesticides, including glyphosate, but not 2,4-D. De Roos noted that these types of studies need to consider multiple exposures

- Wigle et al. (1990) looked at records of 70,000 male farmers in Saskatchewan to compare mortality records with Census of Agriculture records for pesticide use. They did not find an excess of mortalities among any specific causes of death, but did find dose-dependent increases in NHL risk for acres sprayed in 1970 with herbicides, and dollars spent on fuel and oil
- Pearce and McLean (2005) noted that, "farmers have an increased risk of non-Hodgkin lymphoma (NHL), several studies have found increased risks of NHL among producers or sprayers of pesticides. The findings are markedly inconsistent across countries and studies, but overall there is evidence of an increased risk among production workers and professional pesticide sprayers with heavy exposure." Pearce and McLean summarized 15 studies (and 22 endpoints) of phenoxy herbicides and risk of NHL. They found risk ratios ranging from 0.9 to 4.9, with only five of the endpoints with significant 95 percent confidence intervals lower bounds of over 1.0. The range of CIs among the studies was between 0.4 and 27.0. Pearce and McLean concluded that an increased risk of NHL due to phenoxy exposure was uncertain. They also noted that exposure to arsenic, solvents, organophosphate insecticides, organochlorine insecticides, and zoonotic viruses may explain increased risk of NHL among farmers
- Alavanja (2004) reviewed 29 studies examining pesticides and NHL. Alavanja noted that while there is growing evidence for a link, there is no consistent pattern. He evaluated studies of NHL and exposure to phenoxy acetic acids (2,4-D), organochlorine, and organophosphate pesticides. Eighteen of 29 studies had a higher OR for NHL, with an average of 1.3, and a 95 percent CI of 1.17 to 1.55
- Burns et al. (2001) provided a follow-up report on Dow Chemical Company employees that manufactured 2,4-D between 1945 and 1994. The study looked at mortality among these 2,4-D workers compared to other company employees. Burns found no significant risk for NHL, using a standardized mortality ratio (SMR). The SMR for 2,4-D workers was 1.0 compared to the United States population, and 2.63 (95 percent CI 0.85 to 8.33) compared to other Dow employees
- Kogevinas et al. (1995) examined an international cohort of workers exposed to 2,4-D, 2,4,5-T, and dioxins using data from the IARC. For 2,4-D exposure and STS, with 9 cases and 24 controls, they calculated an OR of 5.72 (95 percent CI of 1.14 to 28.65). The OR for NHL was lower, based on 12 cases and 56 controls, for an OR of 1.11 (95 percent CI of 0.46 to 2.65, i.e. not significant). However, there was a dose-response relationship, with number of NHL cases (and the OR) increasing with increased exposure to 2,4-D
- Bond et al. (1989) report that "the weight-of-evidence currently available does not support a conclusion that the phenoxy herbicides present a carcinogenic hazard to humans." They noted that others have not been able to replicate Hardell's studies, and that there have been inconsistent results in various studies. Bond evaluated eight studies, with ORs ranging from 0.8 to 6.8 for soft tissue sarcoma or NHL. Bond noted that uncontrolled confounding could cause the large ORs in Hardell's studies
- McDuffie et al. (2001) conducted a cross-Canada study of pesticides and health and noted that there was elevated risk of NHL with exposure to multiple pesticides. For phenoxy herbicides, the OR was 1.38 (95 percent CI 1.06 to 1.81). For 2,4-D specifically, the OR was 1.32 (95 percent CI 1.01 to 1.73 CI), based on 517 cases and 1,506 controls
- In their weight-of-evidence review, Ibrahim et al. (1991) evaluated case-control studies of 2,4-D, summarizing a number of studies

with varying results (many mentioned above). One of their concerns was that many of the earlier studies were on phenoxy herbicides in general, not just 2,4-D. These studies included 2,4,5-T, which has been banned in most countries. Ibrahim summarizes, "the case-control findings for NHL, taken as a whole, suggest an association with use of phenoxy herbicides, although the evidence is not entirely consistent. Less clear but still suggestive is the evidence for an association between NHL and exposure to 2,4-D." They also noted, "one cannot dismiss the possibility that 2,4-D has been falsely implicated or that the ORs for 2,4-D are suppressed inappropriately when the adjustments are made for use of other herbicides."

While Ibrahim made these observations in 1991, studies in the seventeen years since do not seem to have clarified the potential linkages between 2,4-D, glyphosate, or pesticides in general, and NHL.

Exposure to Heat

WHCP treatment crews work outdoors during the hottest summer months. Without proper precautions, there is potential for workers to suffer from heat illness. Heat illness is defined as a serious medical condition resulting from the body's inability to cope with a particular heat load, and includes heat cramps, heat exhaustion, heat syncope, and heat stroke (CCR Title 8, Section 3395). In response to a high number of heat-related deaths among outdoor workers in 2005, the State of California implemented Heat Illness Prevention Standards. These regulations outline preventative measures for employers to take to reduce the risk of heat illness among their employees.

CalOSHA, the State's job safety agency, further reviewed heat-related illness in early 2009. This additional review occurred in response to seven deaths and 60 worker injuries during 2008, despite the implementation of the Heat Illness Prevention Standards (Ferriss 2008).

Heat illness covers a range of types and symptoms, ranging from headaches and nausea to death. Heat illness is preventable, but it is important to treat the first signs of heat illness seriously. Symptoms of several types of heat illness, as provided by CalOSHA, are listed below (CalOSHA 2008a):

- **Heat rash** – also called prickly heat, may occur in hot, humid environments where sweat is not easily removed from skin by evaporation. Heat rash can become serious if extensive, or infected
- **Fainting** – also called heat syncope, is a stage of heat stroke. Fainting may occur when a worker not acclimated to heat simply stands still in the heat
- **Heat cramps** – muscle spasms that occur when workers are hydrated, but have not replaced electrolytes lost in sweat
- **Heat exhaustion** – occurs when workers become dehydrated and/or have lost electrolytes. Workers will sweat, but may experience extreme weakness, fatigue, giddiness, nausea, or headache. Skin may become clammy and moist, complexion pale or flushed, and body temperate may be slightly higher than normal
- **Heat stroke** – is the most serious form of heat illness, and can result in death. Heat stroke is caused by the failure of the body's internal mechanism to regulate its core temperature. Sweating stops and the body can no longer rid itself of excess heat. Symptoms include: mental confusion, delirium, loss of consciousness, convulsions, coma, and high body temperature (106 degrees Farenheit or more). Skin of heat stroke patients may be hot, dry, red, mottled, or bluish.

California's Heat Illness Prevention Standard includes four steps to preventing heat illness: training, water, shade, and planning. The regulations require employers to provide training on heat illness prevention; provide enough fresh water so that each employee can drink at least one quart per hour (and encourage them to do so); provide access to at least five minutes of rest in the shade when needed for preventative recovery; and develop

and implement written procedures for complying with the heat illness prevention standard. The DBW follows CalOSHA's heat illness prevention guidelines, including the "85 degree" rule to ensure that shade is available and accessible.

CalOSHA encourages employers to proactively address heat illness by monitoring weather conditions, providing additional training on hot days, adjusting work shifts to avoid the heat, and promoting a "buddy system" so that workers can monitor each other (CalOSHA 2008a). CalOSHA also recently published a guide for employees to carry out tailgate training for workers (CalOSHA 2008b).

WHCP treatment crews may be outside during hot weather for extended periods of time. In addition, use of coveralls and other PPE make workers more susceptible to heat illness. Workers may also be more susceptible to heat illness if they have not acclimated to warm temperatures. There is potential for WHCP treatment crews to suffer adverse impacts to their health as a result of exposure to heat during normal WHCP operations.

* * * * *

To minimize exposure to herbicide, WHCP treatment crews are required to utilize personal protective equipment (PPE) as specified on the herbicide labels, and described in the WHCP Operations Management Plan.

WHCP treatment crews are required to follow the PPE requirements specified on the Weedar® 64 label. These requirements are more stringent than those of Aquamaster™. PPE requirements include: coveralls, chemical-resistant gloves, chemical resistant footwear, chemical-resistant headgear for overhead exposure, and protective eye wear. In addition, a chemical-resistant apron should also be worn when cleaning equipment, mixing, or loading. Masks will also be available to treatment crews, if they prefer additional facial protection. Proper use of PPE has been proven to reduce herbicide exposure.

It is extremely unlikely that there would be acute health impacts to WHCP treatment crews as a result of exposure to herbicides. It is also unlikely that there would be chronic health impacts to WHCP treatment crews as a result of exposure to herbicides. However, given the uncertainties related to the long-term human health impacts of low level exposure to 2,4-D and glyphosate, it is important that the DBW minimize the potential for adverse health outcomes as a result of long-term, low-level, exposure of WHCP treatment crews to 2,4-D, and to a much lesser extent, glyphosate. There is also potential for acute health impacts to WHCP treatment crews as a result of heat exposure during WHCP treatments. **These potential impacts to WHCP treatment crew health would be avoidable significant impacts.** These impacts would potentially be avoided, or reduced to a less-than-significant, level by implementing the following five mitigation measures.

- **Mitigation Measure H2a** – Require treatment crews to participate in training on herbicide and heat hazards.

  The DBW will provide training to ensure that treatment crews have the knowledge and tools necessary to conduct the program in a safe manner. Training will include reading, understanding, and following herbicide label requirements; purpose and proper use of PPE; symptoms of herbicide poisoning and minimization of exposure; avoidance, symptoms, and treatment of heat exposure; and emergency medical procedures.

- **Mitigation Measure H2b** – Follow best management practices to minimize the risk of spill, and to minimize the impact of a spill, should one occur.

  The best management practices includes several provisions to reduce the potential for spill, such as: fastening herbicide containers securely in boats in original, watertight containers; carrying a marker buoy and anchor line to mark any spills in water; reporting spills immediately to appropriate State and

local agencies; immediately stopping movement of land spills using absorbing materials; marking and monitoring spills in water for herbicide residues and environmental impacts, if appropriate. Treatment crews will include at least one person with a Qualified Applicators Certificate (QAC), and all crew members will participate in annual training on herbicide handling procedures.

- **Mitigation Measure H2c (same as Mitigation Measures B2c; B4b; W1c, W2c; and W3c)** – Implement an adaptive management approach to minimize the use of herbicides.

  Under an adaptive management approach, DBW will seek to improve efficacy and reduce environmental impacts over time as new and better information is available. Specifically, DBW will evaluate the need for control measures on a site by site basis; select appropriate indicators for pre-treatment monitoring; monitor indicators following treatment and evaluate data to determine program efficacy and environmental impacts; support ongoing research to explore the impacts of the WHCP and alternative control methodologies; report findings to regulatory agencies; and adjust program actions, as necessary, in response to recommendations and evaluations by regulatory agencies and stakeholders. In addition to this adaptive management approach, DBW will follow maintenance control practices that seek to reduce the number of acres of water hyacinth to be treated each year, until treatment acreage reaches a minimal level. This will reduce the volume of herbicide utilized by the WHCP.

- **Mitigation Measure H2d (same as Mitigation Measures B1c; B2d; W1d; W2e; W3e; and A1b)** – Conduct herbicide treatments in order to minimize potential for drift.

  In addition to following the label requirements, DBW will, to the degree possible, schedule herbicide applications to occur at high tide, or at a point in the tidal cycle determined by the field supervisor to provide the least non-target impact at a particular site. In general, treatment at high tide will allow for better spray accuracy and access and will provide for greater dilution volume of herbicides. DBW crews will change nozzle type and spray pressures whenever conditions warrant, limiting the amount of herbicide which may inadvertently contact non-target species.

- **Mitigation Measure H2e** – Implement safety precautions on hot days to prevent heat illness.

  In addition to annual training on heat illness prevention, and compliance with CalOSHA's California Heat Illness Prevention Standard, DBW Field Supervisors will conduct special training sessions on days when weather is expected to be hot. This training will cover the symptoms of heat illness, and immediate actions to take should any symptoms occur. Field Supervisors will cancel treatments if the weather is exceptionally hot. The DBW will also provide bimini tops (shade covers) for WHCP treatment boats.

Impact H3 – Accidental spill: there is potential for the WHCP to create a significant hazard to the public or the environment through reasonably foreseeable upset and accident conditions involving the release of hazardous materials into the environment

A catastrophic spill of either 2,4-D or glyphosate could result in adverse impacts to human health due to exposure of concentrated herbicides. In concentrated form, WHCP herbicides could have acute toxic or corrosive effects if inhaled, ingested, or upon direct contact with skin. Such a spill could also result in adverse impacts to aquatic wetland and intertidal habitat and associated flora and fauna, including special status plants, fish, and wildlife. Impacts could occur to public water supplies, and agricultural production and operations following a spill. The degree of harm would depend on the amount and type of chemical spilled, environmental

conditions (flow, tidal action, weather), and emergency response time.

The DBW's *WHCP Operations and Management Plan* (DBW 2008) identifies best management practices (BMP), including a Spill Contingency Plan (BMP #3). The BMP provides procedures for spill prevention, cleanup, and notification. The DBW follows these procedures to minimize the risk of spill, and to minimize the impact of a spill, should one occur. In 25 years of operation, there have not been any accidental spills of herbicide during WHCP operations.

Should an accidental spill of WHCP herbicides occur, it would represent a significant impact. The potential for the WHCP to result in an accidental spill is **an avoidable significant impact, reduced to a less-than-significant level by implementing the following mitigation measure.**

- **Mitigation Measure H3a (same as Mitigation Measure H2b)** – Follow best management practices to minimize the risk of spill, and to minimize the impact of a spill, should one occur.

  The best management practice includes several provisions to reduce the potential for spill, such as: fastening herbicide containers securely to boats in original, watertight containers; carrying a marker buoy and anchor line to mark any spills in water; reporting spills immediately to appropriate State and local agencies; immediately stopping movement of land spills using absorbing materials; marking and monitoring spills in water for herbicide residues and environmental impacts, if appropriate. Treatment crews will include at least one person with a Qualified Applicators Certificate (QAC), and all crew members will participate in annual training on herbicide handling procedures.

This section identified six mitigation measures to address three potential impacts related to hazards and hazardous materials. One mitigation measure is duplicative, as it applies to two impacts. Two of the mitigation measures, numbers 3 and 7, were also identified in Chapter 3. The remaining four mitigation measures apply specifically to hazards and hazardous materials. **Table 4-5,** below, combines and summarizes the hazards and hazardous materials mitigation measures.

Table 4-5
Summary of Potential Hazards and Hazardous Materials Impacts and Mitigation Measures

	Mitigation Measure Summary[1]	Mitigation Measure Number	Impacts Applied To	Same As Prior Mitigation Numbers
3.	Conduct herbicide treatment in order to minimize potential for drift	Mitigation Measure H2d	Impact H2: Treatment crew exposure	B1c; B2f
7.	Implement an adaptive management approach to minimize the use of herbicides	Mitigation Measure H2c	Impact H2: Treatment crew exposure	B2c; B4b
17.	Minimize public exposure to herbicide treated water	Mitigation Measure H1a	Impact H1: General public exposure	**New**
18.	Require treatment crews to participate in training on herbicide and heat hazards	Mitigation Measure H2a	Impact H2: Treatment crew exposure	**New**
19.	Follow best management practices to minimize the risk of spill, and to minimize the impact of a spill, should one occur	Mitigation Measure H2b Mitigation Measure H3a	Impact H2: Treatment crew exposure Impact H3: Accidental spill	**New**
20.	Implement safety precautions on hot days to prevent heat illness	Mitigation Measure H2e	Impact H2: Treatment crew exposure	**New**

[1] Please refer to the text for the complete mitigation measure description.