# GLYPHOSATE IN REVIEW

June 27, 2018

*Prepared for:*

**Midpeninsula Regional Open Space District**
330 Distel Circle
Los Altos, CA 94022

*Prepared by:*

**Blankinship & Associates, Inc.**
1615 5th Street
Davis, CA 95616

# TABLE OF CONTENTS

# ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| a.e. | Acid equivalent |
| AMPA | Aminomethylphosphonic acid |
| AOP | Adverse outcome pathway |
| ATV | All-terrain vehicle |
| BMP | Best Management Practice |
| CAG | Core Assessment Group |
| CalEPA | California Environmental Protection Agency |
| Cal-IPC | California Invasive Plant Council |
| CARC | USEPA Cancer Assessment Review Committee |
| CDPH | California Department of Public Health |
| CFIA | Canadian Food Inspection Agency |
| CLP | Regulation on the Classification, Labelling and Packaging of Substances and Mixtures |
| District | Midpeninsula Regional Open Space District |
| DPR | California Department of Pesticide Regulation |
| EC | European Commission |
| ECHA | European Chemicals Agency |
| ECI | European Citizens' Initiative |
| EFSA | European Food Safety Authority |
| EU | European Union |
| FAO | Food and Agriculture Organization |
| FDA | U.S. Food and Drug Administration |
| FIFRA | Federal Insecticide, Fungicide, and Rodenticide Act |
| GRAS | Generally Recognized as Safe |
| IARC | International Agency for Research on Cancer |
| IPA | Isopropylamine (salt) |
| IPCS | International Programme on Chemical Safety |
| IPM | Integrated Pest Management |

| | |
|---|---|
| JMPR | Joint FAO/WHO Meeting on Pesticide Residues |
| $K_{OC}$ | Organic carbon binding coefficient |
| $K_{OW}$ | Octanol-water partitioning coefficient |
| LC50 | Median lethal concentration |
| LD50 | Median lethal dose |
| LOAEC | Lowest Observed Adverse Effect Concentration |
| LOAEL | Lowest Observed Adverse Effect Level |
| MCL | Maximum Contaminant Level |
| MOA | Mode of action |
| MRL | Maximum Residue Limit |
| NHL | Non-Hodgkin lymphoma |
| NOAEC | No Observed Adverse Effect Concentration |
| NOAEL | No Observed Adverse Effect Level |
| NOI | Notice of Intent |
| NPDES | SWCRB National Pollutant Discharge Elimination System |
| NSRL | No Significant Risk Level |
| NTP | National Toxicology Program |
| OECD | Organisation for Economic Co-operation and Development |
| OEHHA | Office of Environmental Health Hazard Assessment |
| PCA | Pest Control Adviser |
| PHG | Public Health Goal |
| PMRA | Pest Management Regulatory Agency |
| POD | Point of Departure |
| POEA | Polyethoxylated tallowamine |
| PPE | Personal Protective Equipment |
| Prop 65 | Proposition 65 (Safe Drinking and Toxic Enforcement Act) |
| QAC | Qualified Applicator Certificate |
| QAL | Qualified Applicator License |
| REACH | Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals |

| | |
|---|---|
| REI | Restricted Entry Interval |
| RfD | Reference Dose |
| SAP | FIFRA Scientific Advisory Panel |
| SDS | Safety Data Sheet |
| SURF | DPR Surface Water Monitoring Database |
| SWRCB | State Water Resources Control Board |
| USEPA | U.S. Environmental Protection Agency |
| USFS | U.S. Forest Service |
| WHO | World Health Organization |

# 1. INTRODUCTION

Glyphosate is a nonselective herbicide that can be used for post-emergent applications to over 100 terrestrial food crops as well as non-agricultural sites such as aquatic and residential areas (USEPA, 2017a; 40 CFR § 180.364 ,1997). Since its use first began in 1974, glyphosate has become the most widely used and among the most comprehensively evaluated herbicides. In its more than 40 years of use, it has served as an important agricultural and environmental management tool in more than 160 countries worldwide. In the U.S., total glyphosate use has increased from approximately 1.4 million pounds at the time of its initial registration to 280-290 million pounds in 2014, with agriculture accounting for 90% of use. Given its widespread and extensive history of use, glyphosate has also been the subject of extensive research and repeated safety assessments by regulatory authorities throughout the world.

In Sections 2 through 4 below, the major topics of concern regarding glyphosate are addressed. Its use within Midpeninsula Regional Open Space District's (District's) Integrated Pest Management (IPM) Program is assessed and in Section 5, it's risk is characterized for preserve users and District employees. Recommendations for the District's IPM Program are presented in Section 6.

The active ingredient glyphosate, its potential hazards, and its health effects are the focus of this evaluation. Although some ready-to-use glyphosate-based herbicides are formulated to contain adjuvants and other inert ingredients, the quantity and types of adjuvants and inert ingredients in such products are variable and the available literature regarding toxicity, if any, is limited due in part to the proprietary nature of many of these constituents. Based on the information available, however, the role and significance of adjuvants and inert ingredients and their potential contribution to human health risks associated with the use of glyphosate is addressed.

# 2. HUMAN HEALTH

The human health effects of glyphosate are among the most thoroughly evaluated in the scientific, regulatory and risk assessment literature. It is of critical importance to note that characterization of human health risk can only be evaluated by considering both the degree of exposure and toxicity. The following sections provide a summary of the general background exposure, non-cancer effects, and carcinogenicity findings associated with glyphosate. Based on the toxicity information presented in this section and an evaluation of exposure related to District activities (Section 5.2), the risk associated with District glyphosate use is characterized in Section 5.

## 2.1. Background Exposure

This section presents information on potential exposure to glyphosate resulting from activities other than those of the District activities. Refer to Section 5.2 for a discussion on the potential glyphosate exposures that may result from District activities.

Because glyphosate is registered for use on a variety of agricultural commodities, the U.S. Environmental Protection Agency (USEPA) has established food tolerances for residues of glyphosate resulting from its application. These tolerances represent the limits on the amount of

pesticides that may remain in or on foods marketed in the U.S. and are determined using risk assessment methodology (i.e., by considering both toxicity and exposure data). The food tolerances established for glyphosate range from 0.1 to 300 ppm for different crops (40 CFR § 180.364, 1997) which can also be expressed in units of µg/g and mg/kg. Crops grown for human food and animal feed with glyphosate residues below the established tolerance level are not anticipated to cause substantial adverse health impacts.

Recently, Moms Across America (2017) tested a variety of lunch foods including almond milk, bread, veggie burgers, tea, and peanut butter for residues of glyphosate and aminomethylphosphonic acid (AMPA), the major breakdown product of glyphosate. Of the 11 analyzed product samples, a sample of Lipton® Pure Green Tea was the only product with glyphosate residues (0.19 µg/g) exceeding the lowest tolerance for glyphosate. The concentration of combined glyphosate and AMPA residues in the sample was found to be 0.21 µg/g, which is approximately 5 times lower than the tolerance established for glyphosate in dried tea of 1.0 µg/g.

In another study, a research team from the University of California at San Diego analyzed urinary glyphosate and AMPA levels in 100 people living in a Southern California community who provided samples during clinic visits between 1993 to 1996 and 2014 to 2016 (Mills et al., 2017). Samples were obtained from a population-based investigation known as the Rancho Bernardo Study of Healthy Aging. Approximately 70% of samples taken between 2014 and 2016 had detectable levels of glyphosate and AMPA, while only 12% and 5% of samples taken between 1993-1996 had detectable levels of glyphosate and AMPA, respectively. The authors suggest that the increased prevalence rate observed is likely associated with the increased use of glyphosate since the introduction of genetically modified crops in the U.S. in 1994. From the 1993-1996 period to the 2014-2016 period, average concentrations in urine increased from 0.203 µg/L to 0.449 µg/L for glyphosate and from 0.285 µg/L to 0.401 µg/L for AMPA. Because no other pathways of exposure were presented, the study suggests that consumption of food treated with glyphosate was the primary cause of glyphosate detections in urine. The authors acknowledge the study's limitations due to the cohort being a small population in which an undisclosed subset was examined. No correlation was made between the relationship between chronic glyphosate exposure and human health.

Because District activities do not include the treatment of edible vegetation and it is unlikely that District or preserve users are harvesting and eating treated vegetation, this pathway and the likelihood that District staff or preserve users would have exposure is unlikely.

## 2.2. Non-Cancer Effects

Toxicity for non-cancer effects is measured in a number of ways. In human health risk assessment, toxicity is often characterized by the No Observed Adverse Effect Level (NOAEL)/Concentration (NOAEC). These values represent the highest dose/concentration of a chemical that causes no significant predetermined adverse effects in an experimental population. The lowest dose or concentration of a chemical that causes a significant predetermined adverse effect in an experimental population is referred to as the Lowest Observed Adverse Effect Level (LOAEL) and Lowest Observed Adverse Concentration (LOAEC), respectively. LOAELs and LOAECs are used to describe the first observable signs of chemical-induced toxicity.

While NOAELs, NOAECs, LOAELs, and LOAECs are used as benchmarks for evaluating human health risks associated with individual chemicals, median lethal doses (LD50s) and median lethal concentration (LC50s) are used to broadly categorize general magnitude of toxicity relative to other chemicals. The LD50 or LC50 is the dose or concentration of a chemical that is expected to cause death in 50% of test organisms. LD50s, NOAELs, and LOAELs are typically determined for oral and dermal exposures, while LC50s, NOAECs, and LOAECs are determined for inhalation and drinking water (or dietary) exposures. Chemicals with higher endpoint values (i.e., higher NOAELs, NOAECs, LOAELs, LOAECs, LD50s, or LC50s) are considered to be less toxic relative to chemicals with lower endpoint values. Unlike NOAELs, NOAECs, LOAELs, and LOAECs, however, USEPA uses LD50s and LC50s to classify pesticides such as glyphosate into one of four toxicity categories for each route of exposure: high toxicity (Category I), moderate toxicity (Category II), low toxicity (Category III), or very low toxicity (Category IV).

Glyphosate has very low (Category IV) acute toxicity in mammals through the oral and dermal routes. The LD50 for glyphosate is >5,000 mg/kg/day via oral exposure in rats and >5,000 mg/kg/day via dermal exposure in rabbits (USEPA, 2017a). The oral LD50 in rats is ≥5,000 mg/kg/day and 4,613 mg/kg/day for the isopropylamine (IPA) salt and the ammonium salt, respectively (USEPA, 1993). In rabbits, the dermal LD50 is ≥5,000 mg/kg/day for both salts (Miller et al., 2010). Because its technical form is a nonvolatile solid and adequate inhalation studies of end-use products demonstrate low toxicity, risk associated with the inhalation exposure is expected to be low when glyphosate is used as a pesticide. This is consistent with USEPA's (1993) decision to waive the requirement for an acute inhalation toxicity study and an inhalation toxicity category designation as it relates to the registration of glyphosate-based pesticides. Based on a whole-body exposure study in rats, a 4-hour LC50 of >1.3 mg/L and >1.9 mg/L has been reported for the IPA salt and the ammonium salt, respectively (Miller et al., 2010). Exposure to glyphosate may result in acute eye (temporary corneal opacity or irritation; Category III) or dermal (mild or slight irritation; Category IV) irritation (USEPA, 2017a). Glyphosate is not a dermal sensitizer.

The incidental oral short- and intermediate-term toxicity to glyphosate is characterized by a developmental toxicity study in rabbits. In developmental studies, pregnant experimental animals are exposed to a chemical. Effects experienced by the mother are characterized by the maternal NOAEL/LOAEL, while effects to the developing fetus are characterized by the developmental NOAEL/LOAEL. Chemicals that result in a lower developmental LOAEL than maternal LOAEL are considered developmental toxicants because they elicit toxic responses in fetuses at doses that do not result in maternal toxicity. Rabbits exposed to glyphosate via gavage began to show clinical signs of toxicity (i.e., diarrhea and few or no feces) at the maternal LOAEL of 175 mg/kg/day (USEPA, 2017a). The maternal NOAEL was 100 mg/kg/day while the developmental NOAEL was 300 mg/kg/day. A developmental LOAEL was not established. The same study was also selected by USEPA (2017a) as the critical study for chronic dietary risk assessment and used to establish the Reference Dose (RfD) of 1 mg/kg/day for glyphosate. The RfD is defined as an estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

In a 21-day dermal toxicity study in rabbits, no adverse effects were observed at the limit dose of 1,000 mg/kg/day (USEPA, 2017a). A LOAEL of 5,000 mg/kg/day was established based on

mild erythema and edema on male and female skin and decreased food consumption in females. In another study, rats were exposed to glyphosate via inhalation for six hours per day, five days per week for four weeks (USEPA, 2017a). No adverse effects were observed at the highest concentration tested (0.36 mg/L). Because no dermal toxicity was observed at the limit dose in the dermal toxicity study and no portal of entry effects were observed at the highest concentration tested in the inhalation toxicity study, exposure to glyphosate through these routes is not expected to result in unacceptable risk when label directions are followed. For this reason, USEPA (2017a) did not require quantitative human health risk assessments for the dermal and inhalation risk associated with glyphosate during the registration review process.

In rats administered glyphosate in the diet, no reproductive or developmental toxicity was seen at any dose up to and including the limit dose of 1,000 mg/kg/day (USEPA, 2017a). The maternal LOAEL was not observed, while the offspring LOAEL was observed at the highest dose tested (1,234 mg/kg/day in males and 1,273 mg/kg/day in females) based on delayed age and increased weight at attainment of preputial separation. The offspring NOAEL was 408 mg/kg/day and 423 mg/kg/day in males and females, respectively. In general, the limit dose in acute, subchronic, and chronic toxicity studies is considered adequate to characterize effects that are relevant to human health (FDA, 2010). Based on registered uses in the U.S., pesticide exposures exceeding the limit dose are unlikely to occur outside of test conditions. Like the developmental LOAEL, the reproductive NOAEL was 1,234 mg/kg/day in males and 1,273 mg/kg/day in females. Glyphosate has not been shown to cause adverse effects to nerve tissue (i.e., neurotoxicity) or the immune system (i.e., immunotoxicity) (USEPA, 2017a). Furthermore, weight-of-evidence analyses of endocrine disruption potential indicate that glyphosate does not interact with the estrogen, androgen, or thyroid pathways (USEPA, 2015a).

While individuals may be more likely to be exposed to glyphosate through the dermal and inhalation routes, oral exposure is considered the primary route of glyphosate exposure. Following oral administration, USEPA (2017a) estimates that up to 30-40% of glyphosate can be absorbed by the gastrointestinal tract. Unmetabolized glyphosate is the primary form excreted in urine and feces. In rats given 10 or 1,000 mg/kg/day of glyphosate, 97.5% of the administered dose was excreted as the unchanged parent compound (Williams et al., 2000). Glyphosate is expected to have low tissue retention following dosing and, based on findings that elimination was essentially complete within 24 hours in tested dose ranges, does not bioaccumulate in animal tissue (USEPA, 2017a). Experimental evidence also suggests that its major metabolite AMPA does not bioaccumulate (Williams et al., 2000).

## 2.3. Carcinogenicity

The carcinogenic potential of glyphosate has been evaluated by multiple regulatory and scientific agencies around the world. While many organizations have concluded that glyphosate is not likely to be a carcinogenic risk to humans, others disagree. In the sections below, the carcinogenicity determinations of USEPA, the World Health Organization's (WHO's) International Agency for Research on Cancer (IARC), and other agencies are addressed. A discussion on the evaluation approaches that may contribute to the conflicting viewpoints of these agencies is also provided.

### 2.3.1. USEPA

In 2015, USEPA (2015b) classified glyphosate as “Not Likely to be Carcinogenic to Humans” based on a weight-of-evidence evaluation which points out that tumor incidence in animal carcinogenicity studies was typically only increased at the highest doses tested (≥1,000 mg/kg). Previous assessments by USEPA (1986, 1991) resulted in classifications of “Not Classifiable as to Human Carcinogenicity” and “Evidence of Non-Carcinogenicity for Humans.” Based on its currently registered use patterns, the potential oral exposure of glyphosate for the most highly exposed residential population subgroup (1-2-year-old children) is more than 2,000 times lower than the highest doses tested, while the maximum potential exposure calculated for occupational handlers is more than 140 times lower than the highest doses tested. Because it is considered implausible for humans to be exposed to such excessive dietary doses over time, evidence of carcinogenicity at these levels is not relevant to human health risk assessment.

In subsequent assessments in 2016 and 2017, USEPA (2016, 2017b) concluded that the strongest support based on the weight-of-evidence was still for the “Not Likely to be Carcinogenic to Humans” cancer descriptor, reaffirming its 2015 carcinogenicity determination for glyphosate based on evaluation of additional studies which were not available during the 2015 assessment. Based in part on the results of these carcinogenicity evaluations, USEPA’s proposed interim registration review decision for glyphosate is expected to be published in 2019, including any proposed mitigation measures to reduce unacceptable risk. Refer to Section 3.3 for additional information pertaining to USEPA’s review of glyphosate as a candidate for pesticide registration renewal.

### 2.3.2. IARC

IARC is an intergovernmental agency forming part of the WHO and is one of four WHO programs that have reviewed glyphosate. In 2015, IARC issued a statement that re-classified glyphosate as “probably carcinogenic to humans” (WHO, 2015). This determination was based on “limited evidence of carcinogenicity in humans for non-Hodgkin lymphoma (NHL). The evidence in humans is from studies of exposure, mostly agricultural, in the U.S., Canada, and Sweden published since 2001. In addition, there is convincing evidence that glyphosate can also cause cancer in laboratory animals.” Consequently, glyphosate was added to the Proposition 65 (Prop 65) list by the Office of Environmental Health Hazard Assessment (OEHHA) in 2017 via the Labor Code mechanism. The Labor Code mechanism requires that substances listed as human or animal carcinogens by IARC be listed as known to cause cancer under Prop 65 (HSC § 25249.8, 1986). Under this mechanism, OEHHA does not and “cannot consider scientific arguments concerning the weight or quality of the evidence considered by IARC when it identified these chemicals” (OEHHA, 2015).

### 2.3.3. Other Agencies

IARC’s conclusions that glyphosate is a probable human carcinogen are contrasted by the three other WHO agencies that evaluated glyphosate. These WHO agencies are: the International Programme on Chemical Safety (IPCS), the Core Assessment Group (CAG), and the Guidelines for Drinking-water Quality (WHO, 1994, 2005; WHO and FAO, 2016). Further, the following additional agencies have evaluated glyphosate and have concluded that glyphosate is not likely to be carcinogenic: Health Canada’s Pest Management Regulatory Agency (PMRA,

2017), the European Food Safety Authority (EFSA, 2015), the New Zealand Environmental Protection Authority (NZ EPA, 2016), the European Chemicals Agency (ECHA, 2016), the Australian Pesticides and Veterinary Medicines Authority (APVMA, 2017), the Food Safety Commission of Japan (FSCJ, 2016), and the German Federal Institute of Risk Assessment (BfR, 2015). Despite the consensus among multiple agencies that glyphosate is unlikely to pose a carcinogenic risk to humans, some individual countries in Europe (e.g., France, Sweden) have considered banning glyphosate uses based on the IARC decision (USEPA, 2017b).

#### 2.3.4. Discussion on Evaluation Approach

The conclusions reached by IARC and those reached by other agencies may differ due to diverging evaluation approaches. In the U.S., for instance, some studies included in the IARC evaluation were excluded from USEPA's (2017b) evaluation if they did not collect exposure information on glyphosate from individual subjects, did not assess an outcome (e.g., biomonitoring studies), and/or did not provide a quantitative measure of an association between glyphosate and a cancer outcome. Furthermore, USEPA's (2005) Guidelines for Carcinogen Risk Assessment indicates that the highest dose selected for carcinogenicity studies should elicit toxicity without substantially impacting mortality from non-cancer effects or how the body handles the chemical (e.g., overwhelming absorption and detoxification mechanisms, or reduced consumption of treated food due to poor palatability in dietary studies). In studies where exposure doses are excessively high, tumors may be secondary effects to general toxicity rather than directly attributable to the chemical. For glyphosate, an adequately high dose (i.e., the limit dose) for carcinogenicity studies has been established at 1,000 mg/kg/day (USEPA, 2017b). As such, USEPA puts less weight on observations of increased incidence of tumors that only occur near or above the limit dose (USEPA, 2017b). In contrast, observations of tumors occurring only near or above the limit dose were given equal weight in the IARC evaluation.

Another point of contention is IARC's evaluation of glyphosate formulated products. Health Canada's Pest Management Regulatory Agency (PMRA) points out that while the composition of glyphosate formulated products differs around the world, the IARC assessment relied on many studies that did not characterize the composition of the formulations and/or evaluated all glyphosate formulated products as a group, regardless of their composition (PMRA, 2017). Consequently, the toxicity resulting from such an approach may be caused by contributions from other constituents in the formulation rather than those of glyphosate itself. In some studies, for example, genotoxicity (i.e., damage to cellular genetic material) is observed following exposure to glyphosate formulations but not following exposure to glyphosate alone (USEPA, 2017b). Because such findings suggest that glyphosate formulations may be more toxic than glyphosate alone, USEPA (USEPA, 2017b) intends to evaluate the role of glyphosate in product formulations and the differences in formulation toxicity in future research.

# 3. GLYPHOSATE POLICY UPDATES

Government regulatory agencies worldwide, international organizations, and various scientific institutions and experts have reviewed the available scientific data to make a determination on the safety of glyphosate use as it relates to human health. Additional assessments were prompted by IARC's (2015) evaluation in order to make informed decisions about and

implement modernized policy updates for glyphosate-based pesticides. In this section, recent glyphosate policy updates in Europe, Canada, the U.S., and California are discussed.

## 3.1. Europe

In Europe, products containing glyphosate are commonly used agriculture, horticulture, and in some non-cultivated areas to control weeds that compete with cultivated crops or plants that are otherwise problematic (EC, 2017a). Pursuant to the European Union's (EU's) Regulations on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and on the Classification, Labelling and Packaging of Substances and Mixtures (CLP), glyphosate has been thoroughly evaluated by EU Member States, the European Food Safety Authority (EFSA), and the European Chemicals Agency (ECHA) from 2012 to 2017 to determine whether its use results in any unacceptable effects on humans, animals, or the environment (EC, 2017b).

Following IARC's determination that glyphosate is a probable human carcinogen, the European Commission (EC) mandated the EFSA to review the relevant data in an effort to make a determination on the renewal of glyphosate approval within the EU. In October 2015, EFSA published its conclusion, supported by Member States, that glyphosate is unlikely to pose a carcinogenic hazard to humans; however, additional data was needed to determine its potential endocrine disrupting properties (EC, 2018). This data gap was later addressed in September 2017 based on a weight-of-evidence evaluation indicating that glyphosate does not have endocrine disrupting properties through estrogen, androgen, thyroid, or steroidogenesis pathways (EC, 2017c). Ecotoxicity studies reviewed during the evaluation also supported this finding.

In an independent evaluation, ECHA also determined that, based on available information, glyphosate is unlikely to cause cancer in humans (EC, 2018). ECHA further concluded that glyphosate is neither mutagenic (i.e., capable of causing genetic damage) nor a reproductive toxicant. Despite these findings, some EU Member States such as France and Sweden have considered banning glyphosate uses based on the IARC decision (USEPA, 2017b).

In July 2016, EU Member States voted to amend the conditions of the existing approval of glyphosate in an effort to increase protection of human health and the environment (EC, 2018). Three conditions for further use of glyphosate in the Member States were established: (1) Ban the co-formulant polyethoxylated tallowamine (POEA) from glyphosate formulations; (2) Minimize use in public parks, public playgrounds, and gardens; and (3) Minimize pre-harvest use.

In October the following year, a European Citizens' Initiative (ECI) signed by over 1,000,000 European citizens was submitted to the EC in October 2017 with an aim "to ban glyphosate-based herbicides, exposure to which has been linked to cancer in humans, and has led to ecosystems degradation (EC, 2017b)." In its response, the EC reiterated the findings of ECHA and EFSA that glyphosate should not be classified as carcinogenic, mutagenic, or toxic for reproduction, pointing out that IARC likely reached a different conclusion due to differences in evaluation method. While IARC assessments considered both glyphosate as the active chemical and as part of various formulations, EU assessments focused only on glyphosate. Furthermore, the EU assessment included studies submitted by industry that are not in the public domain. The EC response further stated that, based on EU's ecological risk assessment considering environmental concentrations of glyphosate in various media, glyphosate is not

expected to cause ecosystem degradation when used in accordance with its established conditions of use and "in line with good agricultural practices" imposed by Member States. When necessary, these practices may include mechanisms to reduce ecological impacts associated with agricultural pesticides, such as no-spray zones and use of drift reduction technology.

Based on the findings of EU Member States, EFSA, and ECHA, the EC renewed the approval of glyphosate for five years in December 2017 (EC, 2018). Although EU legislation allows for renewal periods of up to 15 years, a shorter renewal period was granted in light of the rapidly expanding body of knowledge on glyphosate (EC, 2017b). The approval of glyphosate is anticipated to be reassessed in five years; however, reassessment may occur at any time in the event that new scientific evidence indicates that glyphosate no longer satisfies the criteria for herbicide approval in the EU.

## 3.2. Canada

In Canada, glyphosate is registered for use on a wide variety of sites including terrestrial feed and food crops, terrestrial non-food, non-feed and fiber crops, and for non-agricultural, industrial, and residential weed management for non-food sites, forests and woodlots, outdoor ornamentals and turf (PMRA, 2017). Pesticides such as glyphosate are registered by Health Canada's Pest Management Regulatory Agency (PMRA) before they can be imported, sold, or used in Canada. Similar to the pesticide tolerances established by USEPA, PMRA sets Maximum Residue Limits (MRLs) for pesticide residues on food. MRLs represent the maximum amount of residue that is expected to remain on food products when pesticides are used according to label instructions and are set for individual products at levels protective of human health. In 2015-2016 the Canadian Food Inspection Agency (CFIA) tested for glyphosate residues in over 3,000 samples of domestic and imported food products including fresh and processed fruits and vegetables, grains, and bean, pea, lentil, chickpea, and soy products (CFIA, 2017). While glyphosate residues were detected in nearly 30% of samples; the overall compliance rate was 98.7% based on Canadian MRLs. Most samples exceeding the MRLs were associated with grain products.

All pesticides registered for use in Canada are reevaluated by PMRA on a 15-year cycle to determine whether their use continues to meet modern health and environment safety standards. In its recent reevaluation of glyphosate, PMRA (2015) conducted a human health and ecological risk assessment of the active ingredient and formulated products, taking into consideration the potential human health impacts of glyphosate from drinking water, food, and occupational and bystander exposure. In April 2015, PRMA concluded that formulated glyphosate products do not pose unacceptable risks to human health or the environment when used according to revised label instructions. Specifically, PMRA (2015) found that glyphosate is not genotoxic, unlikely to cause a human cancer risk, and unlikely to cause a health risk for individuals exposed via food and drinking water. With the implementation of revised product label directions, undue risks to the environment as well as occupational and non-occupational risks associated with the use of glyphosate are not expected; however, spray buffer zones are necessary to reduce potential risks to non-target organisms such as nearby vegetation, aquatic invertebrates, and fish.

As it pertains to the carcinogenic potential of glyphosate, PMRA (2015) acknowledged that its evaluation was based on different datasets and considerations than that of IARC. The primary difference between the two evaluations was PMRA's use of a weight-of-evidence approach, which gave more weight to studies showing reliable, relevant, and consistent results. Although the active ingredient and its formulated products were both included in the evaluation, studies of glyphosate alone were often given more weight than studies of formulated products. Because formulations contain a variety of inert ingredients that could not be identified due to their proprietary nature, studies of such mixtures were considered less relevant than their glyphosate-only counterparts. Studies conducted in accordance to internationally accepted test guidelines were also considered more relevant and reliable than studies conducted with other methodologies. Furthermore, the PMRA evaluation included several studies not considered by IARC, including industry-supplied lifetime cancer bioassays and mutagenicity studies and epidemiological data.

Based on the 2015 evaluation, PMRA (2017) granted continued registration of glyphosate-based products in Canada, with the requirement that all products implement revised label language by 2019. To minimize human exposure to glyphosate, revised label directions must restrict commercial and residential applicators from using hand-wicking or hand-daubing methods; require a Restricted Entry Interval (REI) of 12 hours for agricultural uses; and indicate that the product is to be applied only when the potential for drift to areas of human habitation or areas of human activity is minimal. To minimize environmental risks associated with the use of glyphosate, revised label directions must: include environmental hazard statements to inform users of toxicity to non-target species; require spray buffer zones to protect non-target terrestrial and aquatic habitats; and include precautionary statements for sites with characteristics or weather conditions that may be conducive to runoff to reduce the potential for runoff to aquatic habitats.

Canada is one of 34 member countries, including the United States, Australia and the EU, within the Organisation for Economic Co-operation and Development (OECD) the routinely collaborate on the regulation of pesticides. As of March 2017, no decision by an OECD member country to prohibit all uses of glyphosate for health or environmental reasons has been identified (PMRA, 2017).

## 3.3. United States

In the U.S., glyphosate is registered to control weeds in various agricultural and non-agricultural settings. As mandated by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), glyphosate is currently undergoing Registration Review. Under this program, the hazards and exposures associated with registered pesticides are reviewed at least every 15 years to determine the potential risks to human and environmental health. Risks are assessed using current practices and policies to ensure pesticide products can still be used safely.

As part of this process, several draft human health and ecological risk assessments have recently been conducted. In September 2015, USEPA's (2015c) preliminary ecological risk assessment found that, while glyphosate residues in water resulting from spray drift or aquatic applications may impact certain non-target aquatic plants (i.e., emergent aquatic vascular plants), exposures are not expected to impact the survival, growth, or reproduction of aquatic invertebrates, fish, aquatic non-vascular plants, or submerged vascular plants. Acute exposure

to glyphosate is not expected to cause unacceptable risk to birds or terrestrial mammals; however, small mammals may be impacted by chronic (generally >10% of the mammal's lifespan) dietary exposure to glyphosate that has been applied to food trees, vines, berries, and small fruit (via ground application up to the maximum combined annual use rate) and in non-agricultural uses such as non-crop areas, forests, and pastures. Exposure at application rates below 1.92 lb a.e./acre for honeybee larvae and below 5.7 lb a.e./acre for adult honeybees are not expected to result in unacceptable risk. Additional toxicity tests are needed to determine risks to terrestrial invertebrates at greater doses.

Because use of glyphosate includes direct applications to potable source waters, this may result in drinking water contamination. USEPA (2017c) conducted a drinking water assessment in 2017 based on label language that defines the maximum allowable glyphosate concentration at the intake of a treated drinking water system as 700 µg/L. In this assessment, the highest estimated glyphosate concentrations in surface source drinking water were associated with aquatic applications in potable water sources. Based on monitoring data, the maximum concentration detected in surface water was 35.1 µg/L. Glyphosate was not expected to impact groundwater during a 100-year simulation. Monitoring data indicated that the median detection frequency of glyphosate was < 0.1%, with a maximum concentration of 2.2 µg/L for groundwater used as a drinking water source.

In a dietary exposure analysis, chronic risk associated with long-term exposure to tolerance-level glyphosate residues in food and drinking water were not of concern for the most highly exposed population (1- to 2-year-old children) (USEPA, 2017d). Quantitative acute and cancer dietary risk assessments were not conducted since appropriate impacts resulting from single-dose exposures were not identified and glyphosate is classified as not likely to be a human carcinogen, respectively.

A residential exposure analysis was also conducted to characterize the risk associated with glyphosate use in non-occupational settings (USEPA, 2017e). Based on the registered turf and aquatic use patterns, USEPA evaluated potential acute dermal and inhalation exposures to residential pesticide handlers and dermal, inhalation, and incidental oral exposures from post-application activities. As mentioned in Section 2.1, USEPA (2017a) does not require quantitative human health risk assessments for dermal and inhalation risk associated with glyphosate due to the low toxicity exhibited through these routes of exposure. Thus, an assessment of the non-occupational incidental oral exposure was conducted to characterize the potential risks to children and swimmers who may have short-term post-application incidental oral exposures from hand-to-mouth behavior on treated turf and from aquatic uses, respectively. No residential risk estimates of concern were identified.

In a human health risk assessment, USEPA (2017a) considered the findings from the dietary and residential exposure analyses to evaluate the total risk from exposures via food, drinking water, and residential use. The resulting aggregate risk estimates were not of concern. While there is potential for acute dermal and inhalation exposures to occupational pesticide handlers and from post-application activities, a quantitative exposure risk assessment was not required due to the low toxicity via these routes of exposure.

The carcinogenic potential of glyphosate has also been extensively reviewed during recent years. Following IARC's determination that glyphosate is probably carcinogenic to humans, USEPA's (2015b) Cancer Assessment Review Committee (CARC) re-evaluated the

carcinogenic potential of glyphosate in accordance with the 2005 Guidelines for Carcinogen Risk Assessment (USEPA, 2005). The assessment included studies reviewed by IARC but which were not previously available to USEPA and concluded that glyphosate is not likely to be carcinogenic to humans.

IARC's evaluation also prompted independent review by EFSA and the Joint Food and Agriculture Organization (FAO)/WHO Meeting on Pesticide Residues (JMPR). While JMPR's evaluation specifically reviewed carcinogenic risk through the diet, both organizations concluded that glyphosate was unlikely to pose a carcinogenic hazard to humans (EFSA, 2015; WHO and FAO, 2016). In 2016, USEPA (2016) issued a follow-up evaluation which included additional relevant studies reviewed in these assessments but which were not previously available to USEPA. A systematic review of the open literature and toxicological databases for glyphosate was also conducted. All studies were evaluated for quality and consistency and given appropriate weight in the evaluation. Based on epidemiological, carcinogenicity, and genotoxicity studies for glyphosate, the determination that glyphosate is not likely to be carcinogenic to humans was retained.

Later in 2016, the FIFRA Scientific Advisory Panel (SAP) was convened to evaluate USEPA's 2016 Issue Paper. In 2017, USEPA (2017b) published a revised Issue Paper incorporating revisions based on FIFRA SAP's evaluation report (USEPA, 2017f) and in addition to recently published carcinogenicity data. Based on available data, USEPA concluded that the strongest support was still for the "Not Likely to be Carcinogenic to Humans" cancer descriptor. However, due to conflicting results and various limitations identified in studies investigating NHL, the risk of NHL onset associated with glyphosate exposure could not be determined. USEPA is currently collaborating with the National Toxicology Program (NTP) Division of the National Institute of Environmental Health Sciences to develop a research plan intended to address data gaps, such as an in-depth understanding of the mode of action (MOA)/adverse outcome pathway (AOP) of glyphosate and how the toxicity of glyphosate formulations is influenced by formulation components (e.g., adjuvants including surfactants, wetting agents, drift retardants, etc.).

USEPA is scheduled to publish the proposed interim registration review decision for glyphosate in 2019. If necessary, the proposed interim registration review decision will outline any proposed mitigation measures to reduce unacceptable risk.

## 3.4. California

In 1986, California voters passed the Safe Drinking and Toxic Enforcement Act, better known as Prop 65 (OEHHA, 2013). Prop 65 requires the State of California publish a list of chemicals known to cause cancer or birth defects or other forms of reproductive harm. These chemicals include a variety of pesticides, food and drugs. Listed chemicals may also be used in or be byproducts of manufacturing, chemical processing, and construction. The list must be updated at least once a year and has accumulated over 800 chemicals since it was first published in 1987.

Prop 65 requires that businesses provide a "clear and reasonable" warning before knowingly and intentionally exposing anyone to a listed chemical. This "right to know" law enables Californians to make informed decisions about protecting themselves from exposure to these chemicals. Prop 65 also forbids businesses from knowingly discharging significant amounts of listed chemicals into sources of drinking water. OEHHA, which is part of the California

Environmental Protection Agency (CalEPA), is the agency responsible for administering the requirements of the law. OEHHA evaluates all currently available scientific information on substances.

Pursuant to the Labor Code listing mechanism, OEHHA (2015) issued a Notice of Intent (NOI) to list glyphosate under Prop 65 in September 2015 following IARC's (2015) determination that glyphosate is "probably carcinogenic to humans." As previously mentioned, this mechanism requires that certain substances identified by IARC be listed as carcinogenic under Prop 65 and prohibits OEHHA from evaluating the scientific merit behind IARC's decision. As such, the Labor Code mechanism is a strictly ministerial process and does not reflect an exercise of discretion or judgment by OEHHA.

Due to the conflicting conclusions of IARC and other agencies such as USEPA, the decision to list glyphosate under Prop 65 has been controversial among the scientific community and strongly opposed by a leading manufacturer of glyphosate formulated products, Monsanto. In January 2016, Monsanto filed a lawsuit against OEHHA in an effort to prevent the glyphosate listing, citing a 2007 risk assessment conducted by OEHHA for purposes of setting a Public Health Goal (PHG) for glyphosate in drinking water. In the assessment, OEHHA (2007) evaluated the same animal carcinogenicity studies included in the IARC evaluation, and found that glyphosate is unlikely to pose a risk of cancer in humans.

The lawsuit claims that by listing glyphosate under Prop 65, OEHHA would be violating Monsanto's right to free speech by requiring it to affix "false and/or misleading" statements to its products. Because the Labor Code mechanism is ministerial in nature and does not allow for OEHHA to reject classification decisions made by IARC, the lawsuit further claims that glyphosate's listing violates Monsanto's right to procedural due process. The lawsuit states that the IARC decision was made by an "unelected, undemocratic, foreign body through a non-transparent process" and was not subject to review by other entities. Despite this criticism, Fresno County Superior Court ruled against Monsanto in March 2017, allowing OEHHA to proceed with the glyphosate listing (Fresno County Superior Court, 2017).

Following this ruling, OEHHA (2017a) posted a Notice of Proposed Rulemaking, proposing to adopt a No Significant Risk Level (NSRL) of 1,100 µg/day for glyphosate. NSRLs represent the amount of a chemical that would result in a cancer risk of no more than 1 in 100,000 for individuals exposed to the chemical over a 70-year time period. Pursuant to Prop 65, products containing chemicals known to cause carcinogenic harm must provide a warning of exposure if they contain levels exceeding the NSRL.

The glyphosate listing under Prop 65 became effective in July 2017 (OEHHA, 2017b); however, in February 2018, a federal judge temporarily dismissed the requirement for Monsanto to print cancer warnings on its products, stating that the warnings would be misleading to ordinary consumers "given the heavy weight of evidence in the record that glyphosate is not in fact known to cause cancer" (Eastern District of California U.S. District Court, 2018). OEHHA (2017c) has previously expressed that in the event that IARC were to change its classification of glyphosate, a reconsideration of the glyphosate listing would be possible.

OEHHA's listing of glyphosate under Prop 65 remains controversial, largely due to the controversial nature in which IARC used data to reach its conclusions and the inability OEHHA has to independently exercise its scientific judgement in making its listing determination. Despite the Prop 65 listing, various groups support continued use of glyphosate. In October 2017, for

example, the California Invasive Plant Council (Cal-IPC) published its position on the issue, stating that it continues to support the use of glyphosate in invasive plant management as part of an IPM approach and that, when used according to the product label with appropriate Personal Protective Equipment (PPE) and Best Management Practices (BMPs), glyphosate is low-risk for wildlife, applicators, and the public (Cal-IPC, 2017).

# 4. ENVIRONMENTAL FATE

The environmental fate of glyphosate-based herbicides is one of the most evaluated and well understood amongst herbicides. The vapor pressure ($<7x10^{-9}$ mmHg; USEPA, 2008) and resultant volatility of glyphosate are very low, minimizing offsite movement during or after application. Its low Henry's Law constant of $<2.07x10^{-12}$ atm-$m^3$/mol (USFS, 2011) indicates that when in water, glyphosate is unlikely to volatilize. Both the low volatility and low Henry's Law constant indicate that glyphosate is not expected to be found in air when label-specific application techniques are employed. Because glyphosate is a broad spectrum, non-discriminatory herbicide, mist produced during glyphosate applications has the potential to impact nearby nontarget vegetation. Therefore, consideration of drift control practices such as the addition of a drift control agent, selection of correct nozzle pressure and selection of appropriate nozzle type is recommended in all cases of glyphosate use. Always read and follow label directions.

Glyphosate is primarily broken down by microbes and fungi in or on the soil and in surface water (Giesy et al., 2000). Other forms of degradation, such as photodegradation (i.e., via sunlight) and hydrolysis (i.e., via water), are not expected to contribute significantly to glyphosate degradation (USEPA, 2008). When glyphosate degrades in soil and water, its primary breakdown product is AMPA (Giesy et al., 2000). AMPA exhibits similar or less toxicity than glyphosate (Borggaard and Gimsing, 2008) and further degrades to naturally-occurring compounds such as carbon dioxide and phosphate. Although this process may result in a contribution of phosphate to an aquatic environment, this contribution is not expected to make a meaningful contribution to nutrients that may be used by aquatic plants and algae.

Glyphosate is very soluble in water (12,000 mg/L; USEPA, 2008) and has a low octanol-water partitioning coefficient ($K_{OW} < 0.00063$; USFS, 2011), indicating that it is not likely to bioaccumulate in animal tissue. In addition to microbial degradation, glyphosate also dissipates in aquatic environments by way of dispersion, dilution when rivers or streams flow into a larger river or lake, and loss through processes such as adsorption to suspended particulate matter or sediments (Giesy et al., 2000). In non-flowing water systems, the rate of glyphosate dissipation may be influenced more heavily by site-specific chemical, physical, and biological conditions. Based on analysis of field and laboratory studies, a conservative range of aquatic half-life values has been estimated to be from 7 to 14 days (Giesy et al., 2000). Half-lives of AMPA are considered comparable to that of glyphosate.

In soil, the rate of glyphosate degradation depends largely on the overall microbial activity of the soil (Carlisle and Trevors, 1988; Moshie and Penner, 1978). The soil metabolism half-life of glyphosate is 1.8 to 5.4 days (USEPA, 2008) under aerobic conditions (i.e., in the presence of oxygen) and 22.1 days (USFS, 2011) under anaerobic conditions (i.e., in the absence of oxygen). Because application scenarios involve application to plants on the ground surface, aerobic conditions are expected to be predominant. Other factors, such as temperature, plant

debris, weather conditions, and soil moisture content contribute to variability in its degradation rate (University of California, Davis, 2010). The dissipation half-life of glyphosate in soils typically ranges from 3 to 174 days (WHO, 1994). A similar range of field dissipation half-lives (2.4 to 160 days) was reported by USEPA (2008). In these studies, glyphosate appeared to persist longer in cold climates than in warm ones.

Based on a meta-analysis of 47 soil degradation studies conducted in diverse soil conditions, the average half-life for glyphosate was estimated to be 32 days (Giesy et al., 2000). The degradation of glyphosate in broom-infested soil in Mt. Tamalpais of Marin County was also investigated by the University of California, Davis (2010). Their study reported glyphosate and AMPA half-lives of 44 and 46 days, respectively. In another terrestrial dissipation study of eight test sites, the median half-life of AMPA was 240 days, with a range of 119 to 958 days (USEPA, 1993). Consistent with its positive charge and like many cations, USEPA reports that there is very little uptake into plants of either glyphosate or AMPA from soil due to their strong binding properties, even immediately after application (40 CFR § 180, 2002). In addition to cationic bonding to soil particles, another important contributing factor in the binding properties of a chemical is often described by its organic carbon binding coefficient ($K_{OC}$), described in Section 4.1 below.

## 4.1. Water Pollution Potential

Glyphosate is not included on the California Department of Pesticide Regulation's (DPR's) Groundwater Protection List, indicating that it is not recognized as a chemical likely to pollute groundwater (3 CCR § 6800, 2014). Chemicals are added to the Groundwater Protection List if they are both mobile (i.e., solubility >3 mg/L, $K_{OC}$ <1,900) and persistent (i.e., hydrolysis half-life >14 days, aerobic soil metabolism half-life >610 days, anaerobic soil metabolism half-life >9 days), and applied in certain ways (i.e., applied to soil via ground-based application equipment or chemigation, or application is followed by flood or furrow irrigation; DPR, 2013a).

Glyphosate's relatively high degradation rate in soil and water, in addition to its strong soil- and sediment-binding potential ($K_{OC}$ = 3,100-58,000; USEPA, 2008), reduces its ability to leach through the soil and into groundwater. While the leaching potential of glyphosate is influenced by factors such as rainfall, soil composition, and drainage type, its vertical movement through soil is generally limited to the top 15 centimeters (USEPA, 1993). This is supported by the fact that glyphosate is not typically detected in groundwater (DPR, 2013b, 2014, 2015, 2016a, 2016b). Between 2004 and 2015, 2,578 wells across up to 38 California counties were sampled for glyphosate by the California Department of Public Health (CDPH) and the State Water Resources Control Board (SWRCB). During this period, no glyphosate detections in groundwater were reported. In a drinking water assessment conducted by USEPA (2017c), glyphosate was not expected to impact groundwater during a 100-year simulation. Monitoring data indicated that the median detection frequency of glyphosate was < 0.1%, with a maximum concentration of 2.2 µg/L for groundwater used as a drinking water source.

The same properties that limit leaching to groundwater (i.e., high degradation rate and high $K_{OC}$) also limit the amount of glyphosate that is transported to surface water via runoff. In a three-year study evaluating glyphosate transport from agricultural fields to surface water, less than 1% of applied glyphosate was typically lost as runoff when the recommended application rate was applied (Edwards et al., 1980). The maximum amount of glyphosate transport by runoff

observed by the study occurred in a field treated at twice the recommended application rate with a severe rainstorm occurring one day after application. Additionally, glyphosate's strong soil-binding potential indicates that, when glyphosate-containing soil particles are washed or blown into surface waters, most of the chemical will remain adsorbed to the particle surface rather than be released into water. Glyphosate-containing soil particles will eventually settle to the bottom of the sediment, where glyphosate is degraded over time by microorganisms (DPR, 1998). Glyphosate has no short- or long-term adverse effects on sediment-dwelling organisms (Simenstad et al., 1996).

Data from DPR's Surface Water Monitoring Database (SURF) indicates that between 1999 and 2017, 477 out of 4,564 surface water samples (10.4%) from California contained detectable concentrations of glyphosate (DPR, 2017). The maximum concentration reported was 1,800 µg/L, and was measured in an agriculture return flow canal immediately after aquatic application of glyphosate (Siemering et al., 2005). All other glyphosate detections reported in SURF were below the PHG of 900 µg/L; all but two glyphosate detections were below the Maximum Contaminant Level (MCL) of 700 µg/L (DPR, 2017; OEHHA, 2017d). PHGs are established by OEHHA and represent the level of a chemical contaminant in drinking water that does not pose a significant risk to health, while MCLs are enforceable standards established by USEPA that represent the maximum allowable amount of a contaminant in drinking water which is delivered to consumers. In USEPA's (2017c) drinking water assessment, the highest estimated glyphosate concentrations in surface source drinking water were similarly associated with aquatic applications in potable water sources. Based on monitoring data, the maximum concentration detected in surface water was 35.1 µg/L.

It should be pointed out the glyphosate is allowed for use in aquatic systems and so its detection after its use is neither surprising nor inconsistent with the product label. Furthermore, the SWRCB National Pollutant Discharge Elimination System (NPDES) permit for residual aquatic pesticide discharges to waters of the United States allows for aquatic use of glyphosate.

# 5. SCREENING-LEVEL RISK EVALUATION

In the following section, the risk of glyphosate applications to pesticide handlers (i.e., District staff) and District preserve visitors is evaluated based on District activities, glyphosate toxicity, and estimated exposure within District preserves. Exposure pathways considered were ingestion, inhalation, and dermal absorption.

## 5.1. District Glyphosate Use

In 2014, the District began implementing an IPM Program to control pests through consistent implementation of IPM principles to protect and restore the natural environment and provide for human safety and enjoyment while visiting and working on District lands. IPM involves using a combination of pest identification and control techniques (i.e., mechanical, chemical, biological, and cultural controls) to manage pest problems while minimizing risks to humans and the environment. As needed, chemical controls such as herbicides are used to manage plants that pose a fire hazard, outcompete native vegetation, are non-native and/or invasive, or are otherwise undesirable.

In 2017, the District utilized two herbicide products containing glyphosate: Roundup® ProMax® (i.e., glyphosate potassium salt) and Roundup® Custom™ (i.e., glyphosate IPA salt). In general, the District uses glyphosate during the spring and summer to manage invasive plants such as yellow starthistle, stinkwort, and French broom. These plants pose a fire hazard when dry and have been rated as having a Moderate to High adverse impact to the ecosystem by Cal-IPC depending on the severity of ecological impacts on physical processes, plant and animal communities, and vegetation structure they impose. Further, if present on or near areas used by preserve visitors, these plants are aesthetically unpleasing and in the case of yellow starthistle, can make trails impassable due to its vigorous and dense growth and sharp thistles. Applications were made by District staff or contractors to small, targeted areas using a backpack sprayer or, for larger areas, a truck- or an all-terrain vehicle- (ATV-) mounted boom sprayer. In total, approximately 77 lb acid equivalent (a.e.) of glyphosate were applied within an area of approximately 170 acres of District property (0.45 lb a.e./acre).

Plant-specific herbicide application rates are described on the product label. After site-scouting to determine the type and density of plant(s) requiring control, specific detail on the application rate, method of application, and other details are presented in a written recommendation prepared by a DPR-licensed Pest Control Adviser (PCA) with expertise in vegetation management. Details addressed in the written recommendation include the criteria used to determine the need for pesticide use; potential hazards and restrictions; crop and site restrictions; notes on the allowable proximity of the application to people, pets, and livestock; and a statement indicating that alternatives and mitigation measures that would substantially lessen any significant adverse impact on the environment have been considered and if feasible, adopted. PCAs must complete no less than 40 hours of continuing education every two years that includes review of laws and regulations and compliance with label directions.

PCAs may also recommend the use of adjuvants to increase efficacy, address tank mix water quality and mitigate drift. In some cases, the use of an adjuvant is required by the product label Currently, the District uses Liberate®, a non-ionic surfactant, when making applications of Roundup Custom.

In addition to the guidance provided by a PCA, the District has implemented a number of BMPs to further reduce human health and environmental risks associated with the use of pesticides. For example, as required by Federal law and reiterated in District BMPs, applicators must follow all label directions when using pesticides. Among other things, this includes the use of PPE and abiding by an REI which prohibits entry into an area of treated vegetation until such time has elapsed that the pesticide cannot be dislodged from the plant surface. District staff also restrict treated areas from public entry until the pesticide has dried. Per label instructions, typical PPE includes a long-sleeved shirt, long pants, shoes, and socks are required for applications of Roundup ProMax and Roundup Custom. Applicators also wear gloves and eye protection in accordance with 3 CCR §§ 6738.1 (2015), 6738.2 (2015), 6738.3 (2016), 6738.4 (2016). For agricultural use, workers are instructed by label language not to enter treated areas during the REI of four (4) hours. For non-agricultural use, people and pets must be kept off treated areas until the pesticide has dried.

All pesticide applicators must hold or be supervised by a person who holds a Qualified Applicator License (QAL) or a Qualified Applicator Certificate (QAC). Like PCAs, QAL/QAC holders are licensed by DPR and trained in techniques to minimize impacts to human health and the environment. QAL/QAC holders are required to obtain 20 hours of continuing education

every two years and may, as needed, recommend additional protective measures beyond what is required by the product label. Furthermore, a written pesticide safety training program is required for training employees who handle pesticides and fieldworkers who may enter treated fields. The training program must meet the requirements described in 3 CCR §§ 6724 (2018) and 6764 (2018), and be presented by a qualified individual annually to pesticide handlers and fieldworkers that do not hold a QAC/QAL.

Other herbicide-related BMPs such buffer zones, use of spray nozzles to reduce drift and posted pesticide application notification requirements are also implemented under the IPM Program. Details can be found in the District's (2014a) Environmental Impact Report and the District's (2014b) IPM Guidance Manual and their respective addenda.

## 5.2. Glyphosate Exposure

Two potentially exposed groups were considered: preserve users and District staff. Based on the manner in which the District uses glyphosate and the associated BMPs that are employed, relevant pathways of exposure are the acute (i.e., short-term) dermal and inhalation routes. Incidental ingestion of glyphosate residues is not expected because it is assumed that neither group intentionally consumes treated vegetation.

Because of the small volume of glyphosate applied, methods of application, areas being treated subject to posting and REIs, and the employment of BMPs, preserve users are not expected to have chronic (i.e., long-term, continuous) exposure to glyphosate by any route of exposure.

Similarly, because of the low frequency of use, methods of application, small volume of material handled and applied, use of PPE and the employment of BMPs, District staff are not expected to have chronic exposure (i.e., long-term, continuous) to glyphosate by any route of exposure.

Acute exposure scenarios to District staff include contacting pesticide residues during pesticide mixing, loading, or application; contacting contaminated vegetation; accidentally wearing contaminated gloves; accidentally ingesting pesticide residues on contaminated skin; and inhaling aerosolized pesticide during application.

Acute exposure to preserve visitors include contact with contaminated vegetation, accidental ingestion of pesticide residues following contact with contaminated vegetation, and inhalation of glyphosate during application by District staff.

### 5.2.1. District Staff

Dermal contact with glyphosate may occur during pesticide mixing, loading, or application; when handling treated vegetation; and by accidentally wearing contaminated gloves. Dermal exposure from pesticide handling activities is greatly reduced by the use of PPE and REIs. Once pesticide residues have dried, transfer to the skin during dermal contact is minimal. Furthermore, glyphosate is poorly absorbed through the skin; the U.S. Forest Service (USFS) estimates a dermal absorption rate of 0.04% per hour (USFS, 2011). Dermal exposure, both by direct contact and contact with contaminated gloves, is therefore considered *de minimis* for this receptor. Because District applicators are either a QAL/QAC or supervised by one, the use of appropriate PPE and adherence to the REI is highly likely and as a result dermal exposure is *de minimis*.

Incidental ingestion of glyphosate may occur if proper PPE is not worn, if hands are not properly washed, if the REI is not adhered to or if proper care is not taken to avoid unintentional transfer of pesticide residues on the skin to the mouth. As mentioned above, all District pesticide applicators must hold or be supervised by someone who holds a QAL/QAC. Because District applicators are QAL/QACs or supervised by one, they are trained not to ingest pesticides, therefore oral exposure is expected to be *de minimis*.

Inhalation exposure of aerosolized glyphosate from the use of application equipment, such as backpack sprayers, may occur during application. As described in Section 4, glyphosate has a low vapor pressure. Inhalation exposure is further reduced due to the District's use of spray nozzle BMPs intended to keep pesticide droplets within the intended spray area. As a result, post-application inhalation exposure is anticipated to be *de minimis*.

#### 5.2.2. Preserve Visitors

Contact with glyphosate residue may occur when preserve visitors brush up against treated vegetation on the application site. Although incidental hand-to-mouth ingestion of glyphosate residue may occur following dermal contact with treated vegetation, the resultant dermal and incidental oral exposures are anticipated *de minimis* due to posting done by the District to restrict access to treated areas and adherence to the pesticide label that states that that people and pets must be kept off treated areas until the pesticide has dried. Once pesticide residues have dried, transfer to the skin during dermal contact is considered *de minimis.* Intentional contact with treated vegetation is similarly anticipated to be *de minimis* based on regulations for use of District lands, which state that no person shall possess, damage, injure, take, place, plant, collect, or remove any plant, fungi, tree, or portion thereof, whether living or dead, including, but not limited to flowers, lichens, mosses, mushrooms, bushes, trees, tree limbs, tree branches, vines, grass, cones, seeds, and deadwood located on District Lands.

Direct contact with glyphosate is not expected to occur due to the District's implementation of application notification BMPs that keep preserve users away from application areas and glyphosate's low dermal absorption rate. Exposure via consumption of treated vegetation is not expected to occur because vegetation being treated with glyphosate is not generally considered edible and is unlikely to be harvested and consumed. While some products containing glyphosate are labeled for use on food crops and some food crops are grown on District property, pesticide application to food crops are not permitted in the District's IPM Program. Thus, ingestion of glyphosate residues on contaminated vegetation is not likely to occur.

Inhalation of glyphosate may occur if preserve visitors are in or near the treatment area during application. Based on the low vapor pressure of glyphosate, District posting and label language indicating that people and pets must stay out of treated areas until glyphosate is dry, and the District's implementation of spray nozzle and application notification BMPs, the potential for inhalation exposure to aerosolized pesticide is *de minimis*.

## 5.3. Glyphosate Toxicity

Refer to Section 2 above for a description of the human toxicity associated with glyphosate. Pesticides such as glyphosate are subject to thorough scientific evaluation in order to be registered for use within the U.S. Human health risk assessments involve evaluating toxicity and relevant exposure data to estimate the risk to human health associated with pesticide use. In

such assessments, a Point of Departure (POD) is established from experimental data and typically corresponds to effects observed near the lower end of a dose-response curve (e.g., NOAEL, LOAEL). PODs are selected for different routes of exposure and used to quantify the risk expected for each exposure pathway.

Based on a study in rabbits in which maternal toxicity (i.e., diarrhea and few or no feces) was observed at the LOAEL of 175 mg/kg/day, a maternal NOAEL of 100 mg/kg/day is available for use as the POD for incidental acute oral exposure to glyphosate. Effects observed in the study were minor and temporary (USEPA, 2017a).

No POD was selected for the acute dietary, dermal, and inhalation routes of exposure due to the low toxicity of glyphosate through these pathways and lack of identified adverse health effects at doses relevant to human health risk assessment (i.e., below the limit dose or highest dose tested).

## 5.4. Adjuvants and Inert Ingredients

Adjuvants are materials that are added to a pesticide solution to enhance its efficacy. Adjuvants may be standalone products that are added to a spray tank containing an herbicide-water mixture (e.g., Liberate) or may be part of a ready-to-use herbicide formulated product (e.g., Roundup ProMax). Adjuvants include materials that perform a variety of functions, including, but not limited to: aiding in water conditioning and pH stabilization in order keep herbicides dissolved in solution; enhancing the penetration of a herbicide into the plant's waxy cuticle layer in order to increase efficacy and limit the amount of herbicide needed; controlling spray drift to limit the amount of herbicide that may travel with wind to non-target locations; and decreasing the surface tension of a herbicide mixture to allow for better deposition and coverage on the plant surface.

Surfactants are a type of adjuvant designed to enhance the absorbing, emulsifying, dispersing, spreading, sticking, wetting, or penetrating properties of an herbicide (Bakke, 2007). When surfactants are used during spray applications, water droplets spread into a thin layer over the leaf surface, increasing contact surface area and allowing herbicides to more readily penetrate through waxy leaf cuticles. Surfactants also aid in controlling spray drift by decreasing the surface tension of the solution. The decreased surface tension serves to reduce the formation of small or fine droplets which are more easily carried by the wind.

Typically, USEPA requires naming only active ingredients on pesticide product labels and Safety Data Sheets (SDSs). In some cases, adjuvants are called "inert ingredients" on a pesticide product label and their identification is often considered proprietary and a "trade secret". In other cases, inert ingredients may be named, but the percent composition may not be specified. Although the details of these inert ingredients are often not available to the public, they are disclosed to and evaluated by USEPA during the pesticide registration process. Unidentified or trade secret inert ingredients contained within registered pesticide formulations have been evaluated by USEPA as not expected to result in unacceptable risk when used according to the product label.

Registration of pesticide products under FIFRA includes a determination that the entire product formulation, including inert ingredients, meets the registration standard under FIFRA Section 3 (USEPA, 2017g). This standard includes demonstrating that there is a lack of unreasonable

adverse effects on humans or the environment. In California, both formulated products and adjuvants sold as standalone products are also evaluated by DPR during a registration process separate from that of USEPA. Although the surfactants contained in Roundup ProMax are not disclosed on the product label or SDS, the surfactant components contained in Liberate, the adjuvant used by the District during Roundup Custom applications, have been broadly identified as lecithin, methyl esters of fatty acids, and alcohol ethoxylates (Liberate Label, 2014). Lecithins are naturally occurring phospholipids that are ubiquitous in biological cell membranes. Like methyl esters of fatty acids, lecithins have very low toxicity and have been approved by the U.S. Food and Drug Administration (FDA) as food grade additives (Bakke, 2007; FDA, 2017). Lecithins have also been categorized as "generally recognized as safe" (GRAS) for human consumption (FDA, 2017). Alcohol ethoxylates are common ingredients in household products such as soaps and detergents and have a range of toxicity between very low to moderate.

In general, risk assessments focus on the herbicide active ingredient, although in some cases it may consider inclusion of herbicide formulations and inert ingredients when sufficient data are available. For numerous herbicide products containing inert ingredients as part of the formulation, the compounds and their percent composition within the product are not explicitly or sufficiently identified on the label or SDS. Additionally, quantitative risk evaluations may only be conducted for chemicals for which toxicity data as well as physical, chemical, and environmental fate properties are available. Because California requires registration on adjuvants as pesticide products but USEPA does not, there is relatively less information available on adjuvants than there is on active ingredients (Cal-IPC, 2015). Without more detailed information, it is not possible to present a comprehensive quantitative risk evaluation on adjuvants and other inert ingredients in this document.

Note that factors limiting glyphosate exposure discussed in Section 5.2 (e.g., PPE, REI, label language) are also applicable to the adjuvants and inert ingredients used with glyphosate. Therefore, similar to glyphosate, no chronic exposure to adjuvants and inert ingredients are anticipated.

USFS conducted a thorough review how surfactants may affect the absorption rate of herbicides through the skin (Bakke, 2007). Based on the available literature, USFS concluded that, for a surfactant to increase the absorption of an herbicide, the surfactant must have a physical effect on the upper layer of the skin. The review also indicated that non-ionic surfactants, which are often required for applications of Roundup Custom, have less of an effect on the skin, and therefore absorption, than cationic or anionic surfactants. Studies suggested that, in contrast to expectation, the addition of surfactants may actually decrease the absorption of herbicides through the skin.

## 5.5. Risk Characterization

Based on the toxicity data available and expected levels of exposure for both District staff and preserve visitors, use of glyphosate as a pesticide within the District's IPM Program is not anticipated to result in adverse effects on human health for any exposure pathway. The available toxicity data indicates that the acute toxicity to humans is extremely limited and that glyphosate is of very low toxicity through all pathways of exposure. Additionally, acute adverse health effects have not been identified through dermal exposure at the limit dose or inhalation exposure at the highest dose tested. Although effects have been observed for the acute oral

pathway, the effects identified are minor and reversible. Chronic health effects are not anticipated as chronic exposure to glyphosate is unlikely to result from District activities.

Although potential for human exposure to glyphosate exists when glyphosate is used within the District's IPM Program for vegetation control, exposure is significantly limited due to a number of mitigating factors including District BMP practices as well as label requirements, which include the use of PPE and observance of an REI. The potential for oral exposure, the most relevant pathway of toxicity for glyphosate, is considered extremely remote within the IPM Program's settings, which currently excludes applications to edible vegetation. The required QAL/QAC training of District staff, posting and notification BMPs, and the limited potential for dried residues to transfer onto the skin further limits the potential of incidental oral exposures.

To the degree that information is available, adjuvants and inert ingredients have been identified and characterized to provide basic background information on their identity and use. Although a more definitive, quantitative evaluation of risk due to adjuvants and inert ingredients cannot be completed with the data available at this time, available information indicates that adjuvants and inert ingredients are not anticipated to appreciably increase the absorption of glyphosate through the skin. Furthermore, implementation of District BMP practices, label requirements, the use of PPE, and observance of an REI taken together limit exposure to glyphosate. Because they are applied together and in the same manner, the conclusion of *de minimis* glyphosate exposure is applicable to adjuvant and inert ingredient exposure. The use of adjuvants and inert ingredients included or mixed with glyphosate products during District IPM activities is therefore not anticipated to result in adverse effects on human health for any exposure pathway.

While exposures to glyphosate, adjuvants and inert ingredients due to District activities are expected to be *de minimis* through all pathways, high-end occupational exposures were also of minimal concern in the USFS (2011) assessment which compared worker exposure estimates to the glyphosate RfD of 2 mg/kg/day. General worker exposure was estimated to be the highest during broadcast treatments and lowest for spot spray treatments; however, even at the highest labeled application rate for terrestrial applications (approximately 8 lb a.e./acre) and without the use of PPE, this exposure was not expected to result in unacceptable risk. Accidental worker exposures to glyphosate via skin contact were associated with doses much lower than those associated with general exposures due to poor dermal absorption and relatively brief period of contact.

# 6. IPM PROGRAM RECOMMENDATIONS

Based on the analysis presented above, no adverse impacts to human health were identified for glyphosate used within the District's IPM Program and therefore no changes to existing mitigation measures are recommended at this time.

However, to proactively protect District water resources, the addition of BMP #32 is suggested:

> *Surface and Groundwater Protection – Applicators shall use BMPs regarding the prevention of drift, runoff, erosion, and water quality impairment. All work shall be in compliance with the 3 CCR § 6800 (Groundwater Protection). When possible, plant covers such as landscaping shall be established on bare soil and hillsides to minimize pesticide and sediment runoff. Pesticides without an aquatic label shall not be applied to permeable soils, soils prone to or with*

> *evidence of erosion without containment strategies (e.g., vegetative buffers, sediment barriers), or in areas where aquatic habitats are located within 15 feet of the application site. In no cases should pesticides be applied to surface water bodies unless appropriate permits are obtained.*

Although impacts to ecological receptors were not addressed in this document, the addition of BMP #33 is also suggested. The purpose of BMP #33 is to address the on-going 'Goby-11" court injunction pertaining to the enhanced the protection of eleven special status species (Alameda whipsnake, bay checkerspot butterfly, California clapper rail (Ridgeway's rail), California freshwater shrimp, California tiger salamander, delta smelt, salt marsh harvest mouse, San Francisco garter snake, San Joaquin kit fox, tidewater goby, and valley elderberry longhorn beetle) that occur within the San Francisco Bay Area:

> *Application of glyphosate and cholecalciferol shall be conducted in accordance with the Goby -11 Injunction (Center for Biological Diversity v. EPA, Case No. 07-2794-JCS (N.D. Cal.), May 30, 2007) in applicable and relevant habitats for those species named in the Injunction that occur within the District. Applicable habitats for each species named in the Injunction are defined in the 2010 court order for the Center for Biological Diversity v. EPA. Because the interim protective measures (i.e., no-use buffer zones adjacent to certain features within certain geographic areas) established in the 2010 order vary depending on the species at issue and the pesticide being used, buffer zones between glyphosate treatment areas and species habitat vary, the USEPA webpage should be consulted: https://www.epa.gov/endangered-species/interim-use-limitations-eleven-threatened-or-endangered-species-san-francisco-bay. In addition, District internal special status species mapping resources, buffer zones established on the CNDDB webpage, and an interactive species location map (https://www.epa.gov/endangered-species/san-francisco-bay-area-map-tool-identify-interim-pesticide-use-limitations) should be consulted. The interim use limitations remain in effects until USEPA completes effects determinations for four pesticides named under the 2015 revised settlement agreement for the Center for Biological Diversity v. EPA. The effects determinations are expected to be completed by 2020.*

Suggested minor modifications to existing District BMPs address herbicide-related practices already being conducted by District staff. These include, for example, using an air gap or anti-siphon device to prevent backflow while loading pesticides into application equipment; conducting transfer/mixing activities away from drain inlets, culverts, wells, areas with porous or erosion-prone soil, or other features that may allow for runoff; not irrigating treatment sites immediately after application unless specified by label requirements; calibrating application equipment; and maintaining sufficient vegetative cover to reduce erosion when applying herbicides.

# 7. CONCLUSIONS

Extensive research on glyphosate within the U.S. and around the world has provided strong lines of evidence that, despite recent concerns over the potential human health and

environmental impacts associated with it use, this use is not anticipated to result in adverse effects on human health when label directions are followed. Although glyphosate has been characterized as a probable human carcinogen by IARC, the current consensus among numerous national and international regulatory agencies including other WHO programs and USEPA suggests that there appears to be insufficient data to indicate that glyphosate is a human carcinogen. Glyphosate remains approved for use in the United States, Canada, and the European Union. In the U.S., glyphosate is currently undergoing Registration Review and a proposed interim registration review decision for glyphosate is expected to be published in 2019.

Due to its low human toxicity and limited exposure when used as an herbicide in the District's IPM program, glyphosate is not anticipated to result in adverse effects to District staff or preserve visitors.

Glyphosate can be used with adjuvants and inert ingredients to improve its efficacy. Because of a lack of available information, a comprehensive quantitative risk analysis on adjuvants and inert ingredients was not possible. Because they are applied together and in the same manner and numerous BMPs exist to reduce exposure, the conclusion of *de minimis* glyphosate exposure is applicable to adjuvant and inert ingredient exposure. Therefore, the use of adjuvants and inert ingredients is not anticipated to result in adverse effects on human health for any exposure pathway.

Although no adverse impacts to human health are anticipated, additions and updates to the District's IPM Program BMPs will serve to proactively protect District water resources and threatened and threatened species.

# 8. REFERENCES

Australian Pesticides and Veterinary Medicines Authority (APVMA). 2017. Final regulatory position: Consideration of the evidence for a formal reconsideration of glyphosate. Armidale, Australia.

Bakke, D. 2007. Analysis of Issues Surrounding the Use of Spray Adjuvants With Herbicides. Available: https://www.fs.usda.gov/Internet/FSE_DOCUMENTS/fsbdev3_045552.pdf (Accessed: March 29, 2018).

Borggaard, O.K. and A.L. Gimsing. 2008. Fate of glyphosate in soil and the possibility of leaching to ground and surface waters: a review. Pest Management Science 64, 441-456.

California Department of Pesticide Regulation (DPR). 1998. Environmental Fate of Glyphosate. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2013a. Guidelines for Identifying Pesticides to be Added to and Removed from the Groundwater Protection List: Title 3, California Code of Regulations Section 6800(b). Memorandum. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2013b. Sampling for Pesticide Residues in California Well Water. 2012 Update. Twenty-seventh Annual Report Pursuant to the Pesticide Contamination Prevention Act. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2014. Sampling for Pesticide Residues in California Well Water. 2013 Update. Twenty-eighth Annual Report Pursuant to the Pesticide Contamination Prevention Act. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2015. Sampling for Pesticide Residues in California Well Water. 2014 Update. Twenty-ninth Annual Report Pursuant to the Pesticide Contamination Prevention Act. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2016a. Sampling for Pesticide Residues in California Well Water. 2015 Annual Report. Pursuant to the Pesticide Contamination Prevention Act. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2016b. Sampling for Pesticide Residues in California Well Water. 2016 Annual Report. Pursuant to the Pesticide Contamination Prevention Act. California Environmental Protection Agency. Sacramento, CA.

California Department of Pesticide Regulation (DPR). 2017. Surface Water Monitoring Database (SURF). California Environmental Protection Agency. Available http://www.cdpr.ca.gov/docs/emon/surfwtr/surfdata.htm (Accessed: October 26, 2017).

California Invasive Plant Council (Cal-IPC). 2015. Best Management Practices (BMPs) for Wildland Stewardship. California Invasive Plant Council. Berkeley, CA.

California Invasive Plant Council (Cal-IPC). 2017. Cal-IPC Fact Sheet and Position Statement: The Use of Glyphosate for Invasive Plant Management. Available: http://www.cal-ipc.org/wp-content/uploads/2017/11/Cal-IPC-glyphosate-policy.pdf (Accessed: November 14, 2017).

Canadian Food Inspection Agency (CFIA). 2017. Safeguarding with Science: Glyphosate Testing in 2015-2016. Ottawa, Ontario.

Carlisle, S.M. and J.T. Trevors. 1988. Glyphosate in the environment. Water, Air, and Soil Pollution 39:409-420.

Eastern District of California U.S. District Court. 2018. Memorandum and Order Re: Motion for Preliminary Injunction for *National Association of Wheat Growers; National Corn Growers Association; United States Durum Growers Association; Western Plant Health Association; Iowa Soybean Association; South Dakota Agri-Business Association; North Dakota Grain Growers Association; Missouri Chamber of Commerce and Industry; Monsanto Company; Associated Industries of Missouri; Agribusiness Association of Iowa; Croplife America; and Agricultural Retailers Association v. Lauren Zeise, in Her Official Capacity As Director of the Office of Environmental Health Hazard Assessment; and Xavier Becerra, in His Official Capacity as Attorney General of the State of California* (Case 2:17-cv-02401-WBS-EFB).

Edwards, W.M., G.B. Triplett, and R.M. Kramer. 1980. A watershed study of glyphosate transport in runoff. Journal of Environmental Quality 9(4):661-665.

European Chemicals Agency (ECHA). 2016. Proposal for Harmonised Classification and Labelling. Substance Name: N-(phosphonomethyl)glycine; Glyphosate (ISO). Dortmund, Germany.

European Commission (EC). 2017a. Frequently Asked Questions: Glyphosate. Available: https://ec.europa.eu/food/sites/food/files/plant/docs/pesticides_faq_glyphosate_20170719_final.pdf (Accessed: February 15, 2018).

European Commission (EC). 2017b. Communication from the Commission on the European Citizens' Initiative "Ban glyphosate and protect people and the environment from toxic pesticides". Available: http://ec.europa.eu/transparency/regdoc/rep/3/2017/EN/C-2017-8414-F1-EN-MAIN-PART-1.PDF (Accessed: February 15, 2018).

European Commission (EC). 2017c. Commission Implementing Regulation (EU) 2017/2324 of 12 December 2017 renewing the approval of the active substance glyphosate in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. Official Journal of the European Union 333: 10-16.

European Commission (EC). 2018. Glyphosate. Available: https://ec.europa.eu/food/plant/pesticides/glyphosate_en (Accessed: February 15, 2018).

European Food Safety Authority (EFSA). 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA Journal. 13(11): 1-107.

Fieldworker Training, 3 CCR § 6764 (2018).

Food and Drug Administration (FDA). 2010. Guidance for Industry: M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals. U.S. Department of Health and Human Services. Washington, D.C.

Food and Drug Administration (FDA). 2017. Select Committee on GRAS Substances (SCOGS) Opinion: Lecithin and Lecithin, Hydrogen Peroxide Bleached. Available: http://wayback.archive-it.org/7993/20180124002145/https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260453.htm (Accessed: March 30, 2018).

Food Safety Commission of Japan (FSCJ). 2016. Glyphosate Summary. Cabinet Office, Government of Japan. Tokyo, Japan.

Fresno County Superior Court. 2017. Stipulation and [Proposed] Order and Judgement for *Monsanto Company v. Office of Environmental Health Hazard Assessment, et al*. (Case No.: 16CECG00183).

German Federal Institute of Risk Assessment (BfR). 2015. Does glyphosate cause cancer? BfR Communication No 007/2015, 23 March 2015. Available: http://www.bfr.bund.de/cm/349/does-glyphosate-cause-cancer.pdf (Accessed: February 9, 2018).

Giesy, J.P., S. Dobson, and K.R. Solomon. 2000. Ecotoxicological risk assessment for Roundup (R) Herbicide. Reviews of Environmental Contamination and Toxicology 167: 35-120.

Glyphosate; Pesticide Tolerances, 40 CFR § 180 (2002).

Glyphosate; tolerance for residues, 40 CFR § 180.364 (1997).

Groundwater Protection List, 3 CCR § 6800 (2014).

Handler Training, 3 CCR § 6724 (2018).

International Agency for Research on Cancer (IARC). 2015. IARC Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. Available: http://www.iarc.fr/en/media-centre/iarcnews/pdf/MonographVolume112.pdf (Accessed: February 23, 2018).

International Agency for Research on Cancer (IARC). 2017. IARC Monographs Volume 112: Some Organophosphate Insecticides and Herbicides. World Health Organization. Lyon, France.

Liberate Label. 2014. Loveland Products. Greely, CO.

List of Chemicals Known to Cause Cancer or Reproductive Toxicity, HSC § 25249.8 (1986).

Midpeninsula Regional Open Space District (District). 2014a. Final Environmental Impact Report for the Midpeninsula Regional Open Space District Integrated Pest Management Program. Los Altos, CA.

Midpeninsula Regional Open Space District (District). 2014b. Midpeninsula Regional Open Space District Integrated Pest Management Program Guidance Manual. Los Altos, CA.

Miller, A., J.A. Gervais, B. Luukinen, K. Buhl, and D. Stone. 2010. Glyphosate Technical Fact Sheet. National Pesticide Information Center, Oregon State University Extension Services. Available: http://npic.orst.edu/factsheets/archive/glyphotech.html (Accessed: February 9, 2018).

Mills, P.J., I. Kanta-Korwel, J. Fagan, L.K. McEvoy, G.A. Laughlin, and E. Barrett-Connor. 2017. Excretion of the Herbicide Glyphosate in Older Adults Between 1993 and 2016. JAMA 318(16): 1610-1611.

Moms Across America. 2017. Lunch Food Test Results. Available: https://www.momsacrossamerica.com/lunch_food_test_results (Accessed: February 19, 2018).

Moshie, L.J. and D. Penner. 1978. Factors influencing microbrial degradation of $^{14}$C-glyphosate to $^{14}CO_2$ in soil. Weed Science 26:686-691.

New Zealand Environmental Protection Authority (NZ EPA). 2016. Review of the Evidence Relating to Glyphosate and Carcinogenicity. Wellington, New Zealand.

Office of Environmental Health Hazard Assessment (OEHHA). Public Health Goals for Chemicals in Drinking Water: Glyphosate. California Environmental Protection Agency. Sacramento, CA.

Office of Environmental Health Hazard Assessment (OEHHA). 2013. Proposition 65 in Plain Language. California Environmental Protection Agency. Available: https://oehha.ca.gov/media/downloads/proposition-65/general-info/p65plain.pdf (Accessed: March 11, 2018).

Office of Environmental Health Hazard Assessment (OEHHA). 2015. Notice of Intent to List Chemicals by the Labor Code Mechanism: Tetrachlorvinphos, Parathion, Malathion, Glyphosate. California Environmental Protection Agency. Sacramento, CA.

Office of Environmental Health Hazard Assessment (OEHHA). 2017a. Notice of Proposed Rulemaking: Amendment to Section 25705, Specific Regulatory Levels Posing No Significant Risk: Glyphosate. California Environmental Protection Agency. Sacramento, CA.

Office of Environmental Health Hazard Assessment (OEHHA). 2017b. Glyphosate Listed Effective July 7, 2017, as Known to the State of California to Cause Cancer. California Environmental Protection Agency. Available: https://oehha.ca.gov/proposition-65/crnr/glyphosate-listed-effective-july-7-2017-known-state-california-cause-cancer (Accessed: February 19, 2018).

Office of Environmental Health Hazard Assessment (OEHHA). 2017c. RE: Petition for Reconsideration of the Proposition 65 Listing of Glyphosate Pursuant to the Labor Code Mechanism. California Environmental Protection Agency. Available: https://oehha.ca.gov/media/downloads/proposition-65/crnr/comments/letterphilipmiller06262017.pdf (Accessed: February 19, 2018).

Office of Environmental Health Hazard Assessment (OEHHA). 2017d. Glyphosate. Available: https://oehha.ca.gov/chemicals/glyphosate (Accessed October 25, 2017).

Personal Protective Equipment Exemptions, 3 CCR § 6738.4 (2016).

Personal Protective Equipment Use, 3 CCR § 6738.1 (2015).

Pest Management Regulatory Agency (PMRA). 2015. Proposed Re-evaluation Decision: Glyphosate. Health Canada. Ottawa, Ontario.

Pest Management Regulatory Agency (PMRA). 2017. Re-evaluation Decision: Glyphosate. Health Canada. Ottawa, Ontario.

Selection of Protective Eyewear, 3 CCR § 6738.2 (2015).

Selection of Gloves, 3 CCR § 6738.3 (2016).

Siemering, G., J. Hayworth, and A. Melwani. 2005. Aquatic Pesticide Monitoring Program Final Report. SFEI Contribution Number 392. San Francisco Estuary Institute, Oakland, CA.

Simenstad, C.A., J.R. Cordell, L. Tear, L.A. Weitkamp, F.L. Paveglio, K.M. Kilbride, K.L. Fresh, and C.E. Grue. 1996. Use of Rodeo® and X-77® Spreader to Control Cordgrass (Spartina alterniflora) in a Southwestern Washington Estuary: 2. Effects on Benthic Microflroa and Invertebrates. Environmental Toxicology and Chemistry 15(6):969-978.

University of California, Davis. 2010. Environmental Decay of Glyphosate in Broom-Infested Mt. Tamalpais Soils. Department of Civil and Environmental Engineering. Davis, CA. Available: https://www.marinwater.org/DocumentCenter/View/244 (Accessed: May 5, 2014).

U.S. Environmental Protection Agency (USEPA). 1986. A Set of Scientific Issues Being Considered by the Agency in Connection with the Registration Standard for Glyphosate. Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel, Office of Pesticides and Toxic Substances. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 1991. Second Peer Review of Glyphosate. Carcinogenicity Peer Review Committee, Office of Pesticides and Toxic Substances. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 1993. Reregistration Eligibility Decision (RED): Glyphosate. Office of Prevention, Pesticides, and Toxic Substances. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2005. Guidelines for Carcinogen Risk Assessment. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2008. Risks of Glyphosate Use to Federally Threatened California Red-legged Frog (*Rana aurora draytonii*). Office of Pesticide Programs. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2015a. EDSP: Weight of Evidence Analysis of Potential Interaction with the Estrogen, Androgen or Thyroid Pathways: Glyphosate. Office of Pesticide Programs. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2015b. Evaluation of the Carcinogenic Potential of Glyphosate. Office of Pesticide Programs. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2015c. Preliminary Ecological Risk Assessment in Support of the Registration Review of Glyphosate and Its Salts. Office of Chemical Safety and Pollution Prevention. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2016. Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. Office of Pesticide Programs. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017a. Glyphosate. Draft Human Health Risk Assessment in Support of Registration Review. Office of Chemical Safety and Pollution Prevention. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017b. Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. Office of Pesticide Programs. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017c. Drinking Water Assessment for the Registration Review of Glyphosate. Office of Chemical Safety and Pollution Prevention. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017d. Glyphosate. Dietary Exposure Analysis in Support of Registration Review. Office of Chemical Safety and Pollution Prevention. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017e. Glyphosate. Amended Residential Exposure Assessment for a Registration Review. Office of Chemical Safety and Pollution Prevention. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017f. FIFRA Scientific Advisory Panel Meeting Minutes and Final Report No. 2017-01. A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: EPA's Evaluation of the Carcinogenic Potential of Glyphosate. Washington, D.C.

U.S. Environmental Protection Agency (USEPA). 2017g. Pesticide Registration Manual: Chapter 8 – Inert Ingredients. Available: https://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-8-inert-ingredients (Accessed: March 27, 2018).

U.S. Forest Service (USFS). 2011. Glyphosate Human Health and Ecological Risk Assessment: Final Report. Washington, D.C.

Williams, G.M., R. Kroes, I.C. Munro. 2000. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regulatory Toxicology and Pharmacology 31: 117-165.

World Health Organization (WHO) and Food and Agriculture Organization of the United Nations (FAO). 2016. Report of the special session of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 9–13 May 2016. Geneva, Switzerland.

World Health Organization (WHO). 1994. Environmental Health Criteria 159: Glyphosate. International Programme on Chemical Safety. Geneva, Switzerland.

World Health Organization (WHO). 2005. Glyphosate and AMPA in Drinking-water. Guidelines for Drinking-water Quality. Geneva, Switzerland.

World Health Organization (WHO). 2015. IARC Monographs Volume 112: evaluation of five organophosphate insecticides and herbicides. Available: https://www.iarc.fr/en/media-centre/iarcnews/pdf/MonographVolume112.pdf (Accessed: February 9, 2018).