# Appendix G

Toxicity Evaluation for the
UC Berkeley Hill Campus Wildland
Vegetative Fuel Management Plan

# Toxicity Evaluation for the UC Berkeley Hill Campus Wildland Vegetative Fuel Management Plan

Prepared for Ascent Environmental, Inc.
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## Introduction – Herbicide Overview

This document has been prepared to evaluate the herbicides proposed for use by University of California, Berkeley in the Wildland Vegetative Fuel Management Plan (WVFMP or Plan) by analyzing the potential for direct and indirect effects from herbicide use to human health, wildlife, and the environment. Because of UC Berkeley's careful use of the chemicals listed in this document, it is expected that exposures will be relatively low and not result in adverse effects to applicators or the public.

Throughout this document, the evaluation of risks presented are based on the relationship between documented toxicity of an active ingredient (a.i.) and estimates of possible exposure associated with herbicide application. This is a standard method used to provide an estimated risk of chemicals to human applicators, selected target vegetation and non-target biota.

$$Risk = Fn\ (exposure\ x\ toxicity)$$

*HQ = exposure/acceptable level of toxicity (where 1.0 is the initial point of concern)*

As the exposure level decreases, the margin of safety increases. This approach is typically used in U.S. Environmental Protection Agency (USEPA) risk assessments. A hazard quotient (HQ) is the ratio of a projected level of exposure divided by some index of an acceptable exposure or an exposure associated with a defined risk. As the level of projected exposure decreases, the HQ decreases. Because the parameters used to develop risk estimates generally have a large range of potential values and uncertainties, the use of the HQ of 1.0 is very conservative and usually includes large internal safety factors. As a result, the HQ may be considerably larger than 1.0 and the risk estimates used to determine adverse effects to receptors of concern may not be realistic. In the following evaluations of chemicals used or proposed by UC Berkeley, the values included for HQ and/or toxicity are usually based on laboratory test data that are not particularly realistic when the actual field application scenarios are considered. For this reason, the narratives provided for the herbicides proposed for use under the WVFMP should be considered worst case scenarios.

Even highly hazardous chemicals can have little risk if the potential exposure is minimal. This is the basis for the information on the label provided for a chemical and reflects the ways to minimize potential exposure. The evaluations of toxicity in this document address the potential hazard of each chemical but the potential risk is clearly modified by the careful adherence to the restrictions and recommendations provided on the label and Material Safety Data Sheets (MSDS) provided by the chemical company. Generally, regulators and others tracking potential issues of exposure to toxic chemicals use a concept of the Level of Concern (LOC) which is included in many of the evaluations in this document. This value is a comparison of the expected exposure of a chemical to levels that remain at safe levels. Similar to the HQ, the LOC provides a quick look at the potential risk of an activity that includes the chemical.

This document is intended to provide descriptions and characteristics of the herbicides proposed for use under the WVFMP, as well as quickly accessible tables and definitions with succinct information about the relative hazards of each of the pesticide products proposed for use. This document includes the latest information needed to evaluate the safety of the base chemical, including active ingredients and current formulations. In many cases the formulations of herbicides being evaluated herein have additives such as surfactants and emollients used to increase the effectiveness of the herbicide. The list of herbicides proposed for use under the WVFMP are included in the columns below.

## Herbicides

- Stalker (imazapyr)
- Roundup Pro (glyphosate)
- Transline (clopyralid)
- Surflan AS (oryzalin)
- Snapshot 2.5 T (isoxaben + trifluralin )
- Garlon® 4 Ultra (triclopyr)

## Herbicides Proposed for Use in the WVFMP

Chemical control of annual and biennial weeds includes two strategies to treat different life stages: 1) post-emergent (i.e., direct application of herbicide to eliminate the plant), and 2) pre-emergent (i.e., treatment to prevent the germination of seeds). Herbicides are also classified as either selective or non-selective. Selective herbicides control plants in specific plant families or life stages, while allowing other plants to survive uninjured. Utilizing selective herbicides can be a powerful tool in balancing active management with protecting desirable, native vegetation types. Non-selective herbicides and application methods injure all plant species that are directly exposed to treatment, so should be directed only to the target species. Selectivity may be based on either the chemistry of the herbicide but can also reduce non-target exposures with the timing of the application. All of the herbicides listed above could be used to control invasive plants on natural lands. Application methods would include cut-stump, basal bark, and foliar spray by hand. No aerial or ground broadcast spray applications are proposed under the WVFMP. When herbicides are needed for vegetation control, best management practices recommend direct application to the plant or tree either by hand painting the herbicide directly on to the cambium of the freshly cut tree or plant stump or bottle spritzing, no further than 6 inches away. In order to apply an herbicide to a stump or grass, all of the plant or tree's foliage (leaves, branches, and trunks) must be hand or mechanically cut away until nothing is left but a stump or clump. When glyphosate and triclopyr are applied in this manner, the herbicide is absorbed within the plant or tree's system and does not migrate into the surrounding soil.

## Approach

Descriptions of the chemicals in this document include information currently known about the toxicity, ingredients, and additives associated with each of the chemicals and the potential impact to humans and wildlife. The hazard discussions are based on reports and guidance in USEPA toxicity tables included in chemical regulatory documents and appropriate studies provided in support of chemical registration. Wildlife data published as toxicity estimates are in USEPA registrant files (USEPA 2016) and exposure and toxicity tables in the Wildlife Exposure Handbooks, Volume 1 and 2. Additional documents, including "*Herbicide Use and Wood Chip Application Literature Review*" and "*Screening Level Human Health and Ecological Risk Assessment"* were reviewed and are incorporated herein by reference.

Extensive searches on the chemical properties and toxicity of each of the herbicides proposed for use under the WVFMP were conducted to obtain recent information on potential toxicity and adverse effects to human health and wildlife, including aquatic life. Where recent, relevant information has been identified in in the Agency for Toxic Substances and Disease Registry (ATSDR ToxFAQs chemical fact sheets) and new registration information from USEPA, it is included where appropriate. Examples of some of the available databases and search engines that were considered and queried or referenced are listed below:

- CCRIS (Chemical Carcinogenesis Research Info System);
- CHEMFATE (environmental fate);
- Environmental Peer Reviewed Journals and Publications
- ECOTOX (toxicity to fish and aquatic life);
- EXTOXNET (Extension Toxicology Network's pesticide information project).
- HSDB (Hazardous Substances Data Bank);
- IRIS (Integrated Risk Information System; toxicity to human health);
- Material Safety Data Sheet (MSDS) for each chemical
- National library of Medicine (PubChem); and
- Syracuse Environmental Research Associates (SERA) for Chemicals
- USEPA RED and chemical review databases;
- USEPA Wildlife Exposures Handbook V1 &v2.

All herbicides proposed for control of unwanted vegetation must be evaluated to determine their inherent toxicity and the potential adverse impacts to humans and wildlife. Thousands of studies have been conducted by the manufacturers, research scientists, and regulatory agencies on the current suite of chemicals developed as herbicides. These studies and the reports generated provide the basic information used in this document.

The degree of toxicity of a pesticide determines what precautions must appear on the pesticide label. These should always be considered and followed by the users and include, for example, the signal words (*caution, warning, danger*). As a general rule, most pesticides receive the category "caution" which provides a basic level of care when handling any chemical. Highly toxic chemicals are categorized as "danger" to indicate the level of concern needed when handling such chemicals.

> ***CAUTION*** Products with the signal word CAUTION are lower in toxicity. A "CAUTION" label means the product is slightly toxic if eaten, absorbed through the skin, inhaled, or it causes slight eye or skin irritation.
>
> ***WARNING*** *indicates the pesticide product is moderately toxic if eaten, absorbed through the skin, inhaled, or it causes moderate eye or skin irritation.*
>
> ***DANGER*** *means that the pesticide product is highly toxic by at least one route of exposure. It may be corrosive, causing irreversible damage to the skin or eyes, it may be highly toxic if eaten, absorbed through the skin, or inhaled. Then the word "POISON" must also be included in red letters on the front panel of the product label.*

The label also includes first aid recommendations. The use and type of protective clothing and whether the pesticide may be used only by specially trained and certified applicators (restricted use pesticides).

The potential toxicity characteristics to humans for the chemicals proposed for use under the WVFMP are provided in the table below and as an additional information sheet for use in the field. Because it is neither ethical nor practical to conduct toxicity evaluations using humans, the historic approach has been to substitute rats, rabbits, dogs, and other animals as surrogate test animals. Nearly all data provided in the open literature characterizing chemical effects to humans are based on those surrogate animal studies. In rare cases, accidental and occupational exposures have provided information relating to actual adverse effects on humans. Using these surrogate studies, the USEPA provides an overview of metrics to prioritize potential toxic effects (refer to Table 1).

An important consideration in the hazard characterizations associated with the herbicides proposed for use by the WVFMP is the level of potential risk of handling during applications. At the end of each chemical characterization in this document a discussion is included about the basic parameters that lead to the possible adverse effects (risks) of handling. Although not comprehensive risk evaluations, the discussions provide a general overview of the potential for adverse effects of exposures. To develop the risk characterizations the information in the chemical specific Syracuse Environmental Research Associates (SERA) series was combined with USEPA acute and chronic data to synthesize an overview of the potential adverse effects of exposures. The SERA series are some of the most comprehensive hazard and risk assessments that have been conducted and reported. These assessments are all based on realistic estimates of exposure, with likely dose incorporated into the risk equations. These risk assessments were conducted and reported by SERA and are focused on dozens of chemicals that are used in actual field operations. Much of the information and data used in the following chemical characterizations incorporates basic SERA toxicology and risk data and has been updated and modified to be appropriate for the herbicides proposed for use under the WVFMP.

**Table 1. USEPA Categorizations of Acute Chemical Toxicity**

| Toxicity Study | Category I High Toxicity | Category II Moderate Toxicity | Category III Low Toxicity | Category IV Very Low Toxicity |
|---|---|---|---|---|
| Acute Oral | Up to and including 50 mg/kg | > 50 thru 500 mg/kg | > 500 thru 5000 mg/kg | > 5000 mg/kg |
| Acute Dermal | Up to and including 200 mg/kg | > 200 thru 2000 mg/kg | > 2000 thru 5000 mg/kg | > 5000 mg/kg |
| Acute Inhalation | Up to and including 0.05 mg/liter | > 0.05 thru 0.5 mg/liter | > 0.5 thru 2 mg/liter | > 2 mg/liter |
| Eye Irritation | Corrosive (Irreversible destruction of ocular tissue) or corneal involvement more than 21 days | Corneal involvement or irritation clearing in 8-21 days | Corneal involvement or irritation clearing in 7 days or less | Minimal effects clearing in less than 24 hours |
| Skin Irritation | Corrosive (tissue destruction into the dermis and/or scarring) | Severe irritation at 72 hours (severe erythema or edema) | Moderate irritation at 72 hour (moderate erythema) | Mild or Slight irritation (no irritation or slight erythema) |

Source: USEPA 1998

Many commercially available pesticide products contain additives (surfactants, etc.) so the specific products listed in this appendix are evaluated in the formulations that would likely be used under the WVFMP. In some cases, formulations of chemicals contain additives and/or surfactants which will be identified due to potential toxicological concerns of these additives. Although not directly proposed under the WVFMP, additives will be identified when used as a surfactant and addressed as appropriate.

Potential risk must also include chronic or long-term exposure and potential development of cancer. In many cases, the studies used to evaluate the potential linkages to cancer are based on demographic, epidemiological studies in which the linkage is weak or not statically valid. However, to provide a conservative evaluation of chemicals of concern, these linkages are included in the determination of the cancer classification. Potential toxicity of the chemicals proposed for use under the WVFMP are included in Table 2 and cancer classification are provided in Table 3 below.

## Table 2. Potential Human Toxicity of Chemicals Proposed for Use Under the WVFMP

All data reported for estimates of human toxicity are generally based on extrapolations of laboratory animal studies that include conservative safety factors to assure that adverse effects are not underestimated.

| Product Names | Toxicity Overview |
|---|---|
| **GARLON 4 Ultra**<br>**Triclopyr**<br>triclopyr amine<br>CAS No 55335-06-3 | Garlon 4 Ultra is categorized as a Category III (low toxicity) chemical and has very low toxicity to humans if ingested, but may cause skin irritation, serious eye irritation, and may cause respiratory irritation at high doses and exposures. Prolonged skin contact is unlikely to result in absorption of harmful amounts. No adverse effects are anticipated from single ingestion exposure (USEPA 1998). |
| **Round Up**<br>**Glyphosate**<br>(Roundup Pro)/(RoundupProMax) Isopropylamine salt, potassium salt, dimethylamine salt & diammonium salt<br>CAS No 40465-66-5 | Decades of research has indicated that glyphosate has low toxicity (Category III) if ingested. Skin and eye irritation from exposure is possible. There is no evidence of neurotoxicity, immunotoxicity, or acute toxicity. Reproductive toxicity may occur at very high doses. Recent claims of carcinogenicity (class 2A) were based on animal studies. Substantial evidence finds human carcinogenicity unlikely. Some studies suggest that glyphosate may be a possible endocrine-disruptor (USEPA 2017a).[1] |
| **Snapshot 2.5 TG**<br>**Isoxaben**<br>Benzamide, N-[3-1-ethyl- 1-methy propyl)-5- isoxazoly l]-2,6-dimethoxy<br>CAS No:82558-50-7 | Oral toxicity of Snapshot 2.5TG is categorized as very low (Category IV). No adverse effects have been reported for inhalation, but Snapshot 2.5 TG has the potential for minor skin irritation from dust exposure. There are no reports of eye irritation or contact allergy (IRIS 1988). |
| **Snapshot 2.5 TG**<br>**Trifluralin**<br>2,6-Dinitro-N,N-dipropyl-4-(trifluoromethyl)aniline<br>CAS No 1582-09-8 | Oral toxicity of Snapshot 2.5TG is categorized as very low (Category IV). No adverse effects have been reported for inhalation, but Snapshot 2.5 TG has the potential for minor skin irritation from dust exposure. There are no reports of eye irritation or contact allergy (IRIS 1988). |
| **Stalker**<br>**Imazapyr**<br>2-[4,5- dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol- 2-yl]-3-pyridinecarboxylic acid<br>CAS No: 81510-83-0 | Stalker is practically non-toxic (Category III and IV) after ingestion. There are no reports of effects on mammalian reproduction. The chronic estimated level of concern for mammals was not exceeded for any of the registered uses. The chronic risk for mammals is low following all exposure routes to imazapyr. There is no evidence of carcinogenicity, neurotoxicity, or immunotoxicity after exposures to Imazapyr (USEPA 2006). |
| **Surflan AS**<br>**Oryzalin**<br>Benzenesulfonamide, 4-(Dipropylamino)-3,5-Dinitro<br>CAS No 19044-88-3 | Oryzalin generally is of moderate acute toxicity (Category III) but is carcinogenic in animal studies and has been classified as a Group C, possible human carcinogen. (USEPA 1994) |
| **Transline**<br>**Clopyralid,** (Lontrel) (Cody (Alligare) (Confront) (Thistledown) Monoethanolamine salt<br>3,6-dichloro-pyridinecarboxylic acid<br>CAS No 57754-85-5 | Clopyralid has very low toxicity (Category III) if ingested. Clopyralid is classified by the USEPA as "not likely to be a human carcinogen." However, there are some indications of potential birth defects at very high doses. No birth defects were observed in animals given clopyralid at doses several times greater than those expected during normal exposure. Clopyralid is not listed as mutagenic (USDOE 2000, SERA 2004). |

1 There have been court cases involving Roundup in which the juries have awarded several million dollars to plaintiffs. Although glyphosate has been listed under Proposition 65 based on the International Agency for Research on Cancer's (IARC) classification of glyphosate as probably carcinogenic (based on one study in mice), decades of actual laboratory and field testing of glyphosate conclude that glyphosate is not likely to be carcinogenic to humans and no other meaningful risks to human health occur when the product is used according to the label. Recent expert panels have been convened to directly evaluate the claims of the IARC that glyphosate is carcinogenic to humans. Reports of these panels strongly counter that claim and indicate there is insufficient evidence that glyphosate is carcinogenic.

The toxicity data are derived from controlled laboratory animal studies designed to determine the potential adverse effects of the chemical under several possible routes of exposure. Data are derived from each listed USEPA registration sites. Toxicity to other animals and humans based on specific exposure scenarios may be higher or lower, based on additional physical and exposure conditions.

**Table 3. USEPA Cancer Classifications of Chemicals Proposed for Use Under the WVFMP**

| Chemical | Cas No.* | Products | Cancer Classification | USEPA Report Date |
|---|---|---|---|---|
| Triclopyr | 55335-06-3 | Garlon 4 Ultra | Group D--Not Classifiable as to Human Carcinogen. | 5/9/1996 |
| Glyphosate | 1071-83-6 | Roundup Roundup Pro | Not Likely to be Carcinogenic to Humans[1]. | 12/12/2017 |
| Isoxaben | 82558-50-7 | Snapshot 2.5TG | Suggestive Evidence of Carcinogenic Potential. | 10/7/2008 |
| Trifluralin | 1582-09-8 | Snapshot 2.5 TG | Trifluralin is not classifiable as to its carcinogenicity to humans (Group 3). | 4/1/1996 |
| Imazapyr | 81334-34-1 | Stalker | No Evidence of Carcinogenicity. | 12/16/2011 |
| Oryzalin | 19044-88-3 | Surflan AS | Suggestive Evidence of Carcinogenic Potential in animals. | 9/1/1994 |
| Clopyralid | 57754-85-5 | Transline | Not Likely to be Carcinogenic to Humans. | 5/22/2015 |

Source: USEPA OPP Annual Cancer Report 2018, USEPA RED series for Listed Chemicals, USEPA.gov.

1 Although the USEPA has classified glyphosate as not likely to be carcinogenic to humans, it has been listed under Proposition 65 based on the IARC's classification of glyphosate as probably carcinogenic (based on one study in mice). However, decades of actual laboratory and field testing of glyphosate conclude that glyphosate is not likely to be carcinogenic to humans and no other meaningful risks to human health occur when the product is used according to the label. Recent expert panels have been convened to directly evaluate the claims of the IARC that glyphosate is carcinogenic to humans. Reports of these panels strongly counter that claim and indicate there is insufficient evidence that glyphosate is carcinogenic

Although this evaluation provides the documented potential hazards of the chemicals proposed for use by UC Berkeley staff and technicians, the important concept of risk associated with a chemical is the actual exposure (dose) taken in or contacted by the individual. That concept drives the development of best management practices (BMPs) for each herbicide as described on their label and guidance provided by USEPA and other regulatory agencies. Even the most potentially toxic herbicides proposed for use by UC Berkeley would not result in adverse effects or unacceptable risk because the application methods and BMPs that would be implemented would prevent human contact with or intake of the product. This principle is used as the primary operational approach by pesticide applicators during operations and applications.

Each of the herbicides proposed for use by UC Berkeley within the WVFMP area has an extensive series of reports and scientific studies used to determine the relative level of risk associated with exposure. These determinations are provided and supported by the USEPA, European scientific agencies (in a harmonization program) and other public and private groups responsible for the safe use of chemical products. One of the most informative elements of the chemical characterization is a calculated risk estimate where the level of safety is compared to a statistical level of effects, such as 1 in a million. Evaluations for each of the herbicides proposed for use in the WVFMP area are provided below. A simple calculated risk estimate is included in the evaluations using typical lower, central, and upper risk. Although the values are reasonable estimates of the likelihood of risk, they include parameters with large safety and uncertainty factors and are thus generally conservative and overly protective.

# Hazard Evaluations

## Garlon 4 Ultra CAUTION

### Triclopyr

**Several (over 200) retail herbicide products contain the active ingredient**

### Triclopyr

| |
|---|
| Triclopyr mimics auxin, a plant growth hormone, disrupting the normal growth and viability of plants |
| Cut-stump, basal bark, foliar spray |
| Crossbow/Stump Out/Confront/Remedy Ultra/Bonide/Battleship III/4-Speed XT |
| CAS No. 55335-06-3 |
| 3,5,6-trichloro-2-pyridinly)oxy]acetic acid |
| Light yellow to amber liquid, nonflammable, slight odor |
| Triclopyr is not flammable |
| Low human toxicity, eye irritation possible. No evidence of neurotoxicity, carcinogenicity, immunotoxicity or reproductive/developmental toxicity |
| Practically non-toxic to birds, fish, and aquatic invertebrates and bees |

### Mode of Action

Triclopyr is a selective systemic foliar herbicide that moves down to the roots of the vegetation, used primarily to control broadleaf, woody, and herbaceous weeds while leaving grasses and conifers unharmed.

As a selective herbicide, triclopyr affects actively growing plants by mimicking auxin, a plant growth hormone (SERA 1996). Plants rapidly absorb triclopyr through leaves and roots to produce an uncontrolled plant growth and plant death (NPIC 1998). After absorbing the herbicide, plants die slowly (within weeks).

### Environmental Fate and Transport

Ester and salt forms of triclopyr rapidly turn into the triclopyr acid form in the environment, soluble in water, but the ester form is less soluble. Triclopyr has a low vapor pressure. Triclopyr in water breaks down faster with light. The half-life of triclopyr in water with light is around 1 day. Without light, it is stable in water with a half-life of 142 days (USEPA 1998a).

Triclopyr breaks down relatively quickly in soils. It is mainly broken down by microbes. The soil half-life ranges from 8 to 46 days. In deeper soils with less oxygen, the half-life is longer. Triclopyr is mobile in soils. However, movement studies show that triclopyr was not measured in soils deeper than 15 to 90 centimeters (about 6 to 35 inches). The half-life in plants can vary widely with the type of plant. Barley and wheat plants broke down 85% of triclopyr within 3 days of application. The half-life in grass was between 5 and 20 days. The half-life in plants ranges from 3 to 24 days (NPIC 1998).

### Human Toxicology

Human toxicity estimates are extrapolated from animal studies. Triclopyr acid was found to be slightly toxic by oral and dermal routes and has been placed in Toxicity Category III for these effects. Acceptable studies for acute inhalation, primary eye irritation, primary dermal irritation and dermal sensitization were

not available for the technical grade of triclopyr acid. Available data indicate that both Triclopyr triethylamine salt (TEA); and Triclopyr, butoxyethyl ester (BEE); are slightly toxic by oral (Toxicity Category III) and dermal (Toxicity Category III) routes of exposure, and practically non-toxic by inhalation (Toxicity Category IV) and do not cause dermal irritation (USEPA 2014). In a primary eye irritation study triclopyr TEA was found to be corrosive while BEE was found to be minimally irritating. Both TEA and BEE were found to cause dermal sensitization in test animals. The USEPA has classified triclopyr as a Group D chemical that is not classifiable as to human carcinogenicity (DeRoos 2003). Extensive evaluations of triclopyr toxicity suggest that it is low toxicity (USFS 2011).

Technical triclopyr acid was found to be slightly toxic by oral and dermal routes (Toxicity Category III). Acute effects include inhalation, primary eye irritation, primary dermal irritation and dermal sensitization while both BEE and TEA are slightly toxic by oral (Toxicity Category III) and dermal (Toxicity Category III) routes of exposure, and practically non-toxic by inhalation (Toxicity Category IV). They do not cause dermal irritation. These chemicals are classified a Group D chemical (not classifiable as to human carcinogenicity) (NPIC 2018). Triclopyr has not been shown to be an endocrine disruptor (USEPA 1998b; USFS 2011).

### Ecological Toxicology

Triclopyr is practically non-toxic to slightly toxic to birds. Long-term exposures of weeks to months to birds (acid form) may affect eggshell thickness. While the salt form is practically non-toxic to slightly toxic to shellfish, the ester form is moderately to highly toxic. All forms of triclopyr can be toxic to algae.

For fish, the acid and salt forms are practically non-toxic, but the ester form is moderately to highly toxic. The ester form can bioaccumulate (build up) in fish. However, the ester form rapidly degrades to the acid form in the environment and fish are not likely to contact large amounts of the pesticide. A breakdown product of triclopyr is trichlorpropane (TCP) which is slightly to moderately toxic to fish and shellfish. Triclopyr is practically non-toxic to bees.

### Typical Application Scenarios For Triclopyr/Garlon

For terrestrial applications of triclopyr, the main method of application (Table 4 below) is via directed foliar (backpack). Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure, the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates.

### Table 4. Estimates of Potential Risk Synthesized from USEPA data and SERA 2011

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.0003, 0.003, 0.01 | SERA 2011 |

Source: SERA 2011.

**Special Issues Concerning Triclopyr/Garlon**

In light of the various public concerns regarding the use of glyphosate-based products, the President of the University of California (UC), issued a temporary suspension of the use of glyphosate-based herbicides at UC campuses, with four explicit exceptions: 1) fuel-load management programs to reduce wildfire risk, 2) native habitat preservation or restoration activities, 3) agricultural operations, and 4) research activities. The temporary suspension became effective on June 1, 2019. In tandem with the temporary suspension, the UC President established a task force to review UC's current use of glyphosate-based herbicides for vegetation management purposes. The UC Task Force members include faculty and other expert individuals from across the UC system, including the following constituencies: faculty (toxicology, reproductive health, plant sciences, and environmental law); students; Agriculture and Natural Resources; facilities maintenance; groundskeeping; sustainability; environment, health and safety; and the Office of the General Counsel (UCOP 2019). The UC President charged the UC Task Force with several responsibilities, including the preparation of a report addressing the President's directive and providing recommendations for the use of herbicides at UC campuses.

Since convening, the UC Task Force has recommended that pesticides be grouped into three tiers based on hazard. For carcinogenicity, a pesticide is classified as Tier 1 (red-tier/most hazardous) if any one of five identified authoritative bodies identifies the pesticide as a carcinogen. The authoritative bodies include: USEPA, U.S. Food and Drug Administration (USFDA), National Institute for Occupational Safety and Health (NIOSH), the National Toxicology Program (NTP) of the US Department of Health and Human Services (USHHS), and the International Agency for Research on Cancer (IARC). There was not consensus across all members of the UC Task Force on this system of classifying hazard rankings. Two of the UC Task Force members felt that the California Department of Pesticide Regulation (DPR) and the USEPA should be used as the primary authoritative bodies for making hazard classifications. If DPR and USEPA were used, the hazard ranking for Garlon (and glyphosate) would likely change to Tier 2 (medium-tier/yellow) or Tier 3 (low-tier/green). However, because Triclopyr, the active ingredient in Garlon, has been identified as a possible carcinogen by the International Agency for Research on Cancer (IARC), it has been designated Tier 1 by the UC Task Force.

Per the UC President's directive, the Task Force has prepared a report with recommendations regarding the use of pesticides, including:

- The creation of a systemwide integrated pest management (IPM) policy, which requires each UC location to establish a local IPM committee (IPMC).

- All Tier 1 pesticides, including glyphosate and many other pesticides, will be prohibited from all applications except research, unless and until a local IPMC approves a specific use based on a strong justification of necessity and the unavailability of alternative solutions.

- UC will exceed State law with respect to requirements for training in safe pesticide application and licensure of relevant UC staff.

As of early 2020, the UC President accepted all of the Task Force recommendations and UC staff will proceed to implement them expeditiously (UCOP 2020). Therefore, after the UC Berkeley IPMC is established as recommended by the Task Force, UC Berkeley will permit the use of Tier 1 (high-red tier) pesticides, including Garlon, only after the local IPMC has reviewed and approved its specific use application following an IPM based assessment. In addition, regulations for any approved uses of Garlon on the UC Berkeley campus would be more stringent than what is currently required by state law.

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of personal protective equipment (PPE). Because Garlon would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Garlon in excess of USEPA-defined safe levels.

Reasonable estimates of the HQs indicate that workers will not be subject to hazardous levels of triclopyr during applications (TEA at the application rate of 1 lb a.i./acre). For triclopyr BEE, the reasonable estimates of the HQs range from 0.7 to 1.2 based on the chronic reference dose (RfD), which is the dose assigned by USEPA that may result in an adverse effect. At the upper bounds of the estimated exposures for all application methods, the HQs for both triclopyr TEA (HQs = 1.6 to 3) and triclopyr BEE formulations (HQs = 6 to 12) exceed the level of concern (HQ=1), based on the chronic RfD. All of these HQs apply to an application rate of 1 lb a.i./acre and will scale proportionately to the application rate. Adverse developmental effects in experimental mammals have been observed, however, only at high doses that cause maternal toxicity. The available toxicity studies suggest, however, that concern for reproductive effects in humans is not warranted because the doses that elicited the responses were so high that they are not appropriate for human toxicity estimates. (USFS 2011).

Risk characterization estimates for ecological effects at an application rate of 1 lb a.i./acre are likely greater than that would result from typical WVFMP application techniques. Consumption of contaminated vegetation by mammals and birds would likely be considerably less. As with the human health risk assessment, the results suggest the potential for adverse effects, but not overt toxic effects, in large mammals from the consumption of treated vegetation. Because the WVFMP does not propose the use of a broadcast spraying of herbicides, the contamination will be considerably less and the risk to wildlife lower than calculations using 1 lb a.i./acre.

## Roundup Pro CAUTION

### Glyphosate

Several retail herbicide products (>750) contain the active ingredient glyphosate

| |
|---|
| Nonselective post-emergent broad-spectrum weed control |
| Spray application (backpack only) 41% a.i. |
| Roundup Pro/Roundup/Enforcer/Kleeraway/Zep WeedDefeat/Bonide/ Campaign/GroundClear/Killzall/ DuraZone/ Spectracide |
| CAS No 38641-94-0 |
| Isopropylamine salt of N-(phosphonomethyl)glycine Isopropylamine salt of glyphosate |
| Amber-brown, liquid with slight odor. Stable |
| Roundup is not flammable |
| Glyphosate is of relatively low toxicity to mammals and shows no mutagenic or teratogenic potential. Possible link to some cancers with high exposure. It can be an eye and skin irritant, but is not a dermal sensitizer |

### Mode of Action

Glyphosate [N-(phosphonomethyl)glycine] is a nonselective, post-emergent, and systemic herbicide registered for use in agricultural and nonagricultural areas. It is the active ingredient in Aquamaster and Roundup ProMax and is applied to a variety of feed and food crops and agricultural drainage, sewage, and irrigation systems. There are several formulations of glyphosate, including an acid, monoammonium salt,

diammonium salt, isopropylamine salt, potassium salt, sodium salt, and trimethylsulfonium or trimesium salt. Glyphosate is not effective on submerged or mostly submerged foliage and therefore is only applied to control emergent foliage (Schuette 1998; Siemering 2005).

**Environmental Fate and Transport**

Active ingredient Isopropylamine salt of N-(phosphonomethyl)glycine; {Isopropylamine salt of glyphosate} with the additive ethoxylated tallowamine. Identity of other components (37%) is withheld due to trade secret information of Monsanto Company (Monsanto 2017). Roundup products all contain the a.i. glyphosate, but in some formulations, additives are used to enhance the efficacy and usefulness of the applications.

Glyphosate is highly water-soluble. Glyphosate is broken down by microbial degradation to its metabolite aminiomethylphosphonic acid (AMPA) and carbon dioxide. The rate of degradation in water is generally slower than the rate in soil because there are fewer microorganisms in water than in most soils. For all aquatic systems, sediment appears to be the major sink for glyphosate residue. Even though glyphosate is highly water soluble it appears that parent glyphosate and AMPA have a low potential to move to groundwater due to their strong soil adsorptive characteristics (Schuette 1998; Siemering 2005; USEPA 1993). In the soil glyphosate is resistant to chemical degradation, is stable to sunlight, is relatively non leachable, and has a low tendency to runoff (except as adsorbed to colloidal matter and sediment). It is relatively immobile in most soil environments as a result of its strong adsorption to soil particles and does not move vertically below the 6 inch soil layer. Glyphosate's primary route of decomposition in the environment is through microbial degradation in soil.

A Registration Evaluation Decision (R.E.D). was completed for glyphosate by the USEPA (1993), though toxicity and tolerances have been re-evaluated several times as a result of additional chemical uses, as well as new glyphosate salts being registered (FedReg 2007, 2011; USEPA 2006a, 2006b). Glyphosate is poorly biotransformed in rats and is excreted via feces and urine; neither the parent compound nor its major breakdown product bioaccumulates in animal tissue (Williams et al. 2000).

**Human Toxicology**

Human toxicity estimates are extrapolated from animal studies. Glyphosate has been studied for decades and mammalian toxicological data has illustrated the lack of mammalian toxicity. Rat, Oral LD50: > 5,000 mg/kg which is practically non-toxic. Acute dermal toxicity for the rat: LD50: > 5,000 mg/kg practically non-toxic. Skin and eye irritation for rabbits is moderate. Acute inhalation toxicity for rats is practically non-toxic. No skin sensitization for glyphosate acid and no evidence that it is genotoxic. Not carcinogenic in rats or mice. Developmental effects and reproductive effects in rats and rabbits reported only after extreme doses. Numerous recent studies challenge the claims of the IARC that glyphosate is carcinogenic and have revised the toxicity estimates as well (Tarazona et al. 2017). The decades of research with glyphosate support the USEPA regulatory information and continue to indicate that glyphosate is nontoxic to humans when used in compliance with label requirements, and no endocrine disruption is evident (NPIC 2019). Glyphosate products are effective, widely used, generally low risk products for weed control (Gertsberg 2011). Some ancillary reports in the press of sublethal effects on disease resistance, biological diversity, or enzyme activity as a result of ingestion/uptake of glyphosate are interesting but without clear mechanisms that can be related directly to glyphosate (Gertsberg 2011).

The USEPA has classified glyphosate as Category III for oral and dermal toxicity (USEPA 1993), and the isopropylamine and ammonium salts of glyphosate that are used as active ingredients in registered herbicide products exhibit low toxicity to mammals via the oral and dermal routes. Although no scientific evidence had unequivocally indicated that glyphosate is carcinogenic or mutagenic (USEPA 1993), a

recent report by the WHO (WHO 2015) suggests that it "may probably be carcinogenic" although the WHO researchers fail to report a statistically significant finding. Use of the term "probably" generally indicates the linkage is not statistically defensible. The WHO report is a summary of discussions by a panel review convened specifically to update information on several chemicals, including the herbicides tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate, in order to evaluate and update the existing information about the potential for adverse effects.

**Ecological Toxicity**

Aquatic toxicity, fish Rainbow trout (Oncorhynchus mykiss): Acute toxicity, 96 hours, static, LC50: 5.4 mg/L, moderately toxic. Bluegill sunfish (*Lepomis macrochirus*): Acute toxicity, 96 hours, static, LC50: 7.3 mg/L, moderately toxic. Aquatic toxicity, invertebrates Water flea (*Daphnia magna*): Acute toxicity, 48 hours, static, EC50: 11 mg/L, slightly toxic. Mallard duck (*Anas platyrhynchos*): 5 days, LC50: > 5,620 mg/kg diet, practically non-toxic. Bobwhite quail (*Colinus virginianus*): 5 days, LC50: > 5,620 mg/kg diet, practically non-toxic. Honey bee (*Apis mellifera*): Oral/contact, 48 hours, LD50: > 100 µg/bee, practically non-toxic. Earthworm (*Eisenia foetida*): Acute toxicity, 14 days, LC50: > 1,250 mg/kg soil, practically non-toxic. Bioaccumulation Bluegill sunfish (*Lepomis macrochirus*): Fish: BCF: < 1 No significant bioaccumulation has been reported.

The shikimate acid pathway is a metabolic pathway found only in microorganisms and plants, never in animals. Since this pathway is specific to plants and some microorganisms; glyphosate has very low toxicity to mammals. The USEPA classifies glyphosate as Category III for oral and dermal toxicity (USEPA 1993). The oral LD50 for technical grade glyphosate for rats is 4,320 mg/kg. The dermal LD50 for technical grade glyphosate in rabbits is ≥ 2000 mg/kg (USEPA 1993). Technical grade glyphosate is nonvolatile and the LC50 for rats is ≥ 4.43 mg/L based on a 4-hr, nose-only inhalation study (Miller, et al. 2010; USEPA 1993).

The isopropylamine and ammonium salts exhibit low toxicity to mammals via the oral and dermal routes. The oral LD50 for the isopropylamine salt in rats is ≥ 5,000 mg/kg. The oral LD50 for the ammonium salt form in rats is 4,613 mg/kg. The dermal LD50 for rabbits is ≥ 5,000 mg/kg for both salts (Miller, et al. 2010). The salt formulations of glyphosate also exhibit low toxicity via the inhalation route. The 4-hr LC50 for rats exposed to the isopropylamine form is >1.3 mg/L air. The LC50 for rats exposed to the ammonium salt form was >1.9 mg/L in a whole-body exposure (Miller et al. 2010).

A one-year feeding study resulted in no chronic effects in beagle dogs at daily doses of 500 mg/kg. There is no scientific evidence indicating that glyphosate is carcinogenic or mutagenic (USEPA 1993). Experimental evidence has shown that neither glyphosate nor its major breakdown product (aminiomethylphosphonic acid [AMPA]) bioaccumulates in any animal tissue (Williams et al. 2000). Glyphosate is poorly biotransformed in rats and is excreted mostly unchanged in the feces and urine (Williams et al. 2000).

As previously described, glyphosate is practically nontoxic to birds, freshwater fish, and honeybees. Maximum bioconcentration factors were 0.52 times for whole fish (USEPA 1993). Technical grade glyphosate is slightly toxic to practically nontoxic to freshwater invertebratesLC50 values have also been obtained for several species of frogs and the American toad. The 24-hr LC50 for amphibians ranged from 6.6 to 18.1 mg/L. No significant acute toxicity to amphibians was observed with the technical material or the products (e.g., Roundup Original).

**Special Issues Concerning Glyphosate/Roundup**

Regardless of the decades of research indicating that glyphosate is relatively safe when used as designated by USEPA and other regulators, a recent, relevant issue has surfaced for glyphosate, the active ingredient in Roundup. Recent publications (Pahwa et al. 2019) suggest a possible linkage of extreme exposure to Roundup to onset of Non-Hodgkin's lymphoma. However, the preponderance of information and dozens of other studies refute that linkage (Williams et al. 2016; Andreotti et al. 2018). In response to this concern, registration of the glyphosate diammonium salt has been cancelled for two manufacturers (Nu Fam and Syngenta) by the USEPA, but others remain registered for use.

Of all the products proposed for use by UC Berkeley, the one likely to receive the most scrutiny and public concern is glyphosate (specifically as RoundUp) in its many commercial products. Several dozen reports have been reviewed for Roundup and glyphosate due in part to the public concern about the 2015 WHO designation as a Probable Carcinogen and the highly publicized court cases implicating Roundup exposure to the onset of Non-Hodgkins' Lymphoma (NHL). Because of the public concern about the use of Roundup by UC Berkeley, an extensive discussion is provided on the conditions and sequence of investigations on the potential hazards from exposure to Roundup.

Although the role of glyphosate and its hypothetical link to cancer has been the focus of numerous reports in the media and public forums, no clear, unambiguous connection exists between glyphosate exposure and cancer (De Roos 2003). Despite the apparent lack of toxicity to mammals, concerns have been raised by some groups about the possibility that glyphosate may have long-term cancer effects.

In response to the claims that RoundUp and specifically glyphosate "may be responsible for a substantial role in the onset of cancer," the USEPA announced in 2017 that it will not approve labels on products containing glyphosate that link the chemical to cancer. The move was directed at California. In 2017, the state declared the chemical, which is the main active ingredient in the weed killer Roundup, a carcinogen. Roundup producer Monsanto challenged the ruling in federal court, and a judge has temporarily blocked the state from requiring the labels as the lawsuit continues. The revised guidance from USEPA to companies registered to sell products containing glyphosate stipulates that California's labels would "constitute a false and misleading statement" and that the agency will no longer approve labels that contain the state's warning. "We will not allow California's flawed program to dictate federal policy," USEPA Administrator Andrew Wheeler said in a statement supporting the revised regulatory rule. USEPA said the move was based on its numerous internal and contracted studies that show that glyphosate does not pose a public risk when used as directed.

Regardless of the USEPA stance on the lack of correlation between approved uses and NHL cancer, there have been claims of causal connection of glyphosate exposure and this form of cancer. One such claim is the basis of a lawsuit (DeWayne Johnson v. Monsanto Company 2016) against Monsanto, the primary producer of glyphosate. During the trial, the plaintiff indicated that due to an accident during mixing, he was "drenched" with concentrated Roundup. The lawsuit contends that an individual contracted this form of cancer after his continued exposure to glyphosate products, as the person responsible for weed control in his workplace. During the trial, he indicated that he was inadvertently drenched with Roundup/Ranger Pro after an equipment malfunction and was exposed to windblown sprays, a possible misuse of the product based on label guidance. It can be argued that the information in the reports cited and exposures were not sufficient to establish that the individual's cancer was caused by glyphosate. The correlations presented by the prosecutors do not clearly provide causality.

A universal premise in science is "*correlation is not causation*." "Weak correlations between the sporadic exposure to glyphosate and onset of NHL are insufficient to assign a finding of reasonable certainty of the

source of the cancer." (National Association of Wheat Growers et al. v. Lauren Zeise (Director, California Office of Environmental Health Hazard Assessment [OEHHA] and Xavier Becerra [California State Attorney General]).

The juries in the RoundUp cases have awarded several million dollars to the plaintiffs based on little actual demographically supported exposures to the product but are based primarily on studies reported to support the claims of diseases linked to glyphosate exposure. Results that challenge the claims of a disease linkage to glyphosate exposure (Williams et al. 2016) suggest that the claims are not supported by the actual exposure and carcinogenicity data. Of the numerous studies that counter the claim of linkages to diseases, especially cancer, one example using a large multi-state and region evaluation of farm individuals and others, is provided by Koutros et al., 2019 and Mannetje et al 2016. Glyphosate was not statistically significantly associated with cancer at any site, and in this large, prospective cohort study, no association was apparent between glyphosate and any solid tumors or lymphoid malignancies overall, including NHL and its subtypes" (Andreotti et al. 2018).

The overall weight of evidence from the genetic toxicology data supports a conclusion that glyphosate "does not pose a genotoxic hazard and, therefore, should not be considered support for the classification of glyphosate as a genotoxic carcinogen" (Williams et al. 2016). The assessment of the epidemiological data found that the data do not support a causal relationship between glyphosate exposure and NHL. In fact, The American Cancer Society statistics list NHL as approximately 4 percent of all cancers and lists the following risk factors as contributing to development of this cancer: age, gender, ethnicity, geography, family history, as well as possible exposure to certain chemicals and drugs.

In response to the WHO declaration that glyphosate is a "probable carcinogen," numerous scientists have called the designation into question (WHO 2015). It has been shown that the WHO panel ignored negative results available to them. One critical report on the WHO designation is provided by an independent study by four expert panels that did a comparison of the results presented by the WHO panel but included other reports with conflicting conclusions (Williams et al. 2016). The reports and data reviewed by WHO were supplemented by reports and data provided to WHO but not used in their report (reasons for rejection of those data by WHO were not supported by typical scientific discipline):

> "*We decided to remove it because … you couldn't put it all in one paper.*" Aaron Blair, former epidemiologist at the US National Cancer Institute, explaining why new data on glyphosate and cancer were not reviewed or published by the WHO panel (from Williams et al 2016).

Substantial evidence, contrary to the IARC proclamation of carcinogenicity, supports the conclusion that impacts to human health from the use of glyphosate are not significant nor supported by all the data available to the IARC (Koutros et. al. 2019). Conflicting information, suggesting that glyphosate is not carcinogenic, has been reported by the three other WHO agencies, including the WHO International Programme on Chemical Safety, WHO Guidelines for Drinking Water Quality and the WHO Core Assessment Group. Further, a 2018 report by Tarone, who is an accredited statistician, was critical of the IARC findings of glyphosate being a probable carcinogen and indicated that a re-examination of the animal studies cited by IARC resulted in a contrary finding. (Tarone 2018) The author concluded that the data used was scientifically deficient and could not corroborate the finding by the WHO panel on glyphosate. Tarone, and others, including the European Chemicals Agency, reported that the IARC panel highlighted certain positive results from rodent studies, which they relied upon in the deliberations, but ignored contradictory negative results from the same studies, and an inappropriate statistical test was used. The author concluded that when all of the relevant data from the rodent carcinogenicity studies of glyphosate are evaluated together, it is clear that there is not sufficient evidence supporting the notions of

glyphosate as an animal carcinogen. Even a conclusion that there are low levels of animal carcinogenicity would be difficult to support (Tarone 2018). The process of evaluation and registration of herbicides and pesticides used by all applicators, including UC Berkeley, is overseen by the USEPA, which released a draft risk assessment in December 2017 concluding that "glyphosate is not likely to be carcinogenic to humans" (USEPA 2017b).

Trial court cases, especially one decided by a jury, are not the same as scientific consensus. Jurists are not scientists and are dependent upon the information and material provided by the attorneys in court. The USEPA's current draft risk assessment for glyphosate states "The draft human health risk assessment concludes that glyphosate is not likely to be carcinogenic to humans. The Agency's assessment found no other meaningful risks to human health when the product is used according to the pesticide label. The Agency's scientific findings are consistent with the conclusions of science reviews by a number of other countries as well as the 2017 National Institute of Health Agricultural Health Survey" (USEPA 2017a).

Regardless of the disagreement among authoritative bodies on the risks and hazard rankings associated with glyphosate (refer to Table 5), because the IARC has designated glyphosate as a "probable carcinogen," it is considered a Tier 1 pesticide by the UC Task Force (see discussion under "Special Issues Concerning Garlon" above for more information). Therefore, prior to using any glyphosate-based products, UC Berkeley must establish a IPMC and the IPMC must review and approve the proposed uses of glyphosate, following an IPM based assessment. In addition, regulations for any approved uses of glyphosate-based herbicides on the UC Berkeley campus would be more stringent than what is currently required by state law (UCOP 2019, 2020).

**Table 5. Differences of Cancer Classifications of Glyphosate**

| Agency | Carcinogenicity Classification | Classification Definition | Reference |
|---|---|---|---|
| HHS | No Data | The HHS provides no cancer classification for glyphosate | NTP 2016 |
| USEPA | Group D | Group D (not carcinogenic) | IRIS1989 |
| IARC | Group 2A | Group 2A (probable carcinogen} | IARC 2015, 2017 |

Source: WHO 2009. Criteria used to classify chemicals for carcinogenicity are often not the same across regulatory groups and result in differences in their classifications. The IARC has used outlier animal studies to suggest that glyphosate is "probably" carcinogenic so elevates the designation to 2A on the scale. Differences are due to specific criteria in each of the reporting agencies (Portier et al. 2016).

## Typical Application Scenarios For Glyphosate/Roundup

For terrestrial applications of glyphosate, the main application method is directed foliar (backpack); associated risk estimates are shown in Table 6. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure, the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates.

**Table 6. Estimates of Potential Risk Synthesized from USEPA data and SERA 2011**

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.0003, 0.003, 0.01 | SERA 2011 |

Source: SERA 2011.
(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Roundup would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to glyphosate in excess of USEPA-defined safe levels.

Despite the apparent lack of toxicity to mammals, concerns have been raised by some groups about the possible long-term safety of glyphosate. In an animal study, rats and mice were fed a diet containing glyphosate for 13 weeks. The two highest dose groups of male rats (25,000 and 50,000 mg/kg of 99 percent pure glyphosate) had significant reductions in sperm concentrations (Mahler 1992). Female rats in the 50,000 mg/kg group had slightly longer estrus cycles than the control group (Mahler 1992). Glyphosate is included in the final list of chemicals for screening under the USEPA Endocrine Disruptor Screening Program (USEPA 2009a, 2014), which focuses on pesticide active ingredients and inert ingredients with relatively greater potential for human exposure. In all of these studies above, the dose of chemical given to the test animals was far above any reasonably typical exposure in the field and not appropriate as a comparison to use under the WVFMP.

## Snapshot 2.5 TG WARNING

## Isoxaben (*Isoxaben and Trifluralin*)

Several retail herbicide products contain the active ingredient isoxaben.

| |
|---|
| Turf grasses, broadleaf weeds, grasses, vines, and around ornamental shrubs and trees. |
| Cut-stump, basal bark, foliar spray |
| Snapshot 2.5 TG/Gallery 75 DF/TO 2.5 G/Gemini Fortress |
| CAS No 82558-50-7 |
| Isoxaben (N-[3-( 1-ethyl-1-methylpropyl)-5-isoxazolyl] -2,6-dimethoxybenzamide and isomers) |
| White, odorless, occurs as a suspension |
| Isoxaben has very low vapor pressure (1x10-9) and the flash point is not an issue |
| Very low toxicity to humans, non-irritating to eyes or skin. Slight increase in liver tumors possible birth defects in rabbits, no evidence of mutagenicity, or reproductive toxicity. |
| Very acutely toxic to fish, aquatic invertebrates |

### Mode of Action

Isoxaben disrupts the enzymes needed for protein synthesis, preventing growth of unwanted weeds. Isoxaben is a selective preemergent herbicide used primarily to control several broadleaf weeds and

grasses in non-cropland areas. It has pre-emergent efficacy so that it will not control established weeds and must be applied before the unwanted weeds have emerged, during germination. Isoxaben is USEPA registered for use on turf grasses, broadleaf weeds, grasses, vines, and around ornamental shrubs and trees (USEPA 1988).

**Environmental Fate and Transport**

Bioconcentration potential is low (BCF < 100 or Log Pow < 3). Isoxaben biodegrades very slowly in the environment, dependent on the conditions in soil and/or water (Federal Register 2018). Biodegradability: very slow (in the environment). Biodegradation rate may increase in soil and/or water with acclimation.

**Human Toxicity**

Human toxicity estimates are extrapolated from animal studies. Isoxaben is a classified Category III chemical for low toxicity. Products containing isoxaben carry the signal word CAUTION which is associated with low but possible hazard. Isoxaben is classified as a non-carcinogen and very low toxicity if swallowed (IRIS 1998). Harmful effects have not been found from swallowing very small amounts. Acute dermal toxicity has been noted; however, prolonged skin contact is unlikely to result in absorption of harmful amounts. The rat LD50 is > 5,000 mg/kg. No adverse acute effects are anticipated from inhalation nor respiratory irritation (USFS 2000). The rat inhalation LC50 is > 5.71 mg/l. Brief contact is essentially nonirritating to skin and eyes. No evidence of mutagenicity, teratogenicity, or reproductive toxicology. In a standard-based calculation of risk, no adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, isoxaben is not expected to pose an acute risk.

**Ecological Toxicity**

Very highly acutely toxic to aquatic organisms (LC50/EC50 <0.1 mg/L in the most sensitive species). LC50, Oncorhynchus mykiss (rainbow trout), flow-through test, 96 Hour, > 200 mg/l. Acute toxicity to aquatic invertebrates EC50, *Daphnia magna* (Water flea), static test, 48 Hour, 544 mg/l, acute toxicity to algae/aquatic plants (green algae),chronic aquatic toxicity chronic toxicity to fish, chronic toxicity to aquatic invertebrates. Isoxaben is moderately toxic to *Daphnia magna* (Water flea), semi-static test, 0.69 mg/l; Contact LD50, *Apis mellifera* (bees), 100micrograms/bee; LC50, *Eisenia fetida* (earthworms), 14 d, mortality, > 1,000 mg/kg.

**Typical Application Scenarios For Isoxaben/Snapshot**

For terrestrial applications of isoxaben, the main application method is directed foliar (backpack); associated risk estimates are shown in Table 7. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates.

**Table 7. Estimates of Potential Risk synthesized from USEPA data and SERA 2000**

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.003, 0.0003, 0.01 | SERA 2000 |

Source: SERA 2000.
(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Snapshot would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Snapshot in excess of USEPA-defined safe levels.

Based on reasonable conservative estimates of the exposures associated with directed foliar applications, the estimated risk (using the hazard quotient) is well below the level of concern. The lack of an acute RfD or some other similar measure of 'acceptable' short-tern exposure makes it difficult to characterize risk. Accidental exposures for individuals also result in risks below the level of concern. Again, the lack of an acute RfD limits the characterization of risk. Under the conditions of use proposed by the WVFMP, there is no apparent risk in terms of systemic toxicity or reproductive effects for applicators and members of the general public.

Isoxaben is currently registered for uses that could result in short-term residential exposure and the USEPA has determined that it is appropriate to aggregate chronic exposure through food and water with short-term residential exposures to isoxaben. Using the standard USEPA exposure assumptions in risk estimates for short-term exposures, USEPA has concluded the combined short-term food, water, and residential exposures result in an aggregate Margin of Exposure (MOE) of 6,700, for females 13-49 years old. Because EPA's level of concern for isoxaben is a MOE of 100 or below, this MOE is not of concern. (Fed Reg CFR part 180, 2018).

## Snapshot 2.5 TG WARNING

## Trifluralin (*Isoxaben and Trifluralin*)

Several retail herbicide products contain the active ingredient trifluralin

| |
|---|
| Turf grasses, broadleaf weeds, grasses, vines, and around ornamental shrubs and trees. |
| Cut-stump, basal bark, foliar spray by hand |
| Snapshot 2.5 TG/Treflan/Flurene SE/Trust/Triflualina 600/Elancolan Trefanocide/Crisalin/ TR-10/Triflurex/Ipersan |
| Benzenamine, 2,6-Dinitro-N,N-dipropyl-4-(trifluoromethyl) aniline |
| CAS No 1582-09-8 |
| Trifluralin is a yellow-orange crystalline solid not soluble in water. Melting point 48.5-49°C. Used as a selective pre-emergence herbicide. Stable |
| Trifluralin flammability rating is 1 in the index where 5 is high and 1 is low. The flashpoint is well above 185F. |
| Very low toxicity to humans, non-irritating to eyes or skin. Slight increase in liver tumors possible birth defects in rabbits, no evidence of mutagenicity, or reproductive toxicity |
| Very acutely toxic to fish, aquatic invertebrates |

### Mode of Action

Trifluralin's main mechanism of action is the inhibition of cell mitosis. This herbicide typically acts on the meristems and tissues of underground organs, such as roots, epicotyls, hypocotyls, plumules, rhizomes, bulbs and seeds

### Environmental Fate and Transport

Trifluralin is strongly absorbed on soils (Koc = 7,000 g/ml) and nearly insoluble in water. Therefore, leaching and groundwater contamination by trifluralin is not expected to occur. Because adsorption is highest in soils high in organic matter or clay content and once adsorbed, the herbicide is inactive, higher application rates may be required for effective weed control on such soils (USDA 1990).

Trifluralin is subject to degradation by soil microorganisms. Trifluralin remaining on the soil surface after application may be decomposed by UV light or may volatilize. Recommended application rates give season long weed control but fall-seeded grain crops planted in soil treated with trifluralin during the preceding spring were not injured under warm, moist conditions. The half-life of trifluralin in the soil is 45 to 60 days. After six months to one year, 80- 90 percent of its activity will be gone (SERA 2011). Trifluralin is stable under normal temperatures and pressures, but it may pose a slight fire hazard if exposed to high heat or flame. Its flammability rating is 1 (slight) and will not burn spontaneously as its flashpoint is above 185F (NCBI 2017; MSDS, Safety Data Sheet, 2014).

### Human Toxicology

Human toxicity estimates are extrapolated from animal studies. Trifluralin is not acutely toxic to test animals by oral, dermal or inhalation routes of exposure. Pesticide products containing trifluralin may be moderately toxic to relatively non-toxic, depending on the type of formulation. Nausea and severe gastrointestinal discomfort may occur after ingesting trifluralin (USEPA 1989). It may also induce skin allergies and, when inhaled, it may irritate the throat and the lungs.

Most cases of poisoning result from the carrier or solvent in formulated trifluralin products, rather than from the trifluralin itself (NRC Drinking Water and Health 1977). No evidence of mutagenicity was

observed when trifluralin was tested in live animals, and in assays using bacterial and mammalian cell cultures.

USEPA considers trifluralin to be a possible human carcinogen (USEPA 1988, 1989 ). This classification is used when there is limited or uncertain information indicating that a chemical may cause cancer in animals receiving high doses of the chemical.

### Ecological Toxicology

The oral LD50 for technical trifluralin in rats is greater than 10,000 mg/kg, in mice is greater than 5,000 mg/kg, and in dogs, rabbits and chickens is greater than 2,000 mg/kg. However, some formulated products which contain trifluralin may be more toxic than the technical material itself. For example, the oral LD50 for Treflan TR-10 in rats is >500 mg/kg. The dermal LD50 for technical trifluralin in rabbits is >2,000 mg/kg. The administration of 25 mg/kg to dogs for 2 years resulted in no toxicological effects. Studies in the rat and rabbit show no evidence that trifluralin is teratogenic. Meister conducted tests with animals and verified that trifluralin does not have any toxic effect on them when they are exposed to the product either through ingestion, inhalation, or when in contact with the skin. Nausea and severe gastrointestinal discomfort may occur after trifluralin ingestion. When placed in the rabbit eyes, it produced a mild irritation, which was reverted within 7 days.

Trifluralin is not hazardous to birds. The LD50 for bobwhite quail was greater than 2000 mg/kg. The 5-day LC50 in both quail and ducks was greater than 5,000 mg/kg. Trifluralin is toxic to fish and other aquatic organisms. However, its strong adsorption to soil and the usual practice of incorporating trifluralin into the soil at the time of application may prevent exposure of fish to this herbicide. Runoff from fields should be avoided. Trifluralin is toxic to Daphnia, a small freshwater crustacean (USEPA 1987, Fed Reg 1982).

At exposure levels well above label and permissible application rates (100 ppm), trifluralin has been shown to be toxic to earthworms. However, permitted application rates will result in soil residues of approximately 1 ppm trifluralin, a level that had no adverse effects on earthworms (WSSA 1989). In general, trifluralin is not very toxic to higher animals (except fish). It is non-toxic to bees. Trifluralin adsorbed to sediment may pose a risk for fish species that forage by feeding from sediment, particularly since it has a moderate tendency to bioaccumulate.

### Typical Application Scenarios For Trifluralin/Snapshot

For terrestrial applications of trifluralin, the main type of application is directed foliar (backpack); associated risk estimates are shown in Table 8. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates and are illustrated in the table below. Because of the sensitivity of each parameter used to estimate exposure, the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the risk estimates.

### Table 8. Estimates of Potential Risk synthesized from USEPA data and SERA 2007

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution. Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.003, 0.003, 0.03 | SERA 2007a |

Source: SERA 2007.
(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Snapshot would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Snapshot in excess of USEPA-defined safe levels. Non-accidental exposures which may occur during normal applications of trifluralin—the upper bound of HQs for systemic toxicity is 0.03, below the level of concern by a factor of over 30. For carcinogenicity, the HQ is 0.3, below the level of concern by a factor of about 3. An HQ of 1 for carcinogenicity would be associated with a risk of 1 in one million. Thus, an HQ of 3 would be associated with a risk of about 3 in 10 million. At the maximum likely application rate of 2 lbs a.i./acre, the risk would be about 0.6 in one million.

## Stalker CAUTION

### Imazapyr

Several retail herbicide products contain the active ingredient imazapyr

| |
|---|
| Nonselective pre-and post-emergent broad-spectrum weed control |
| Foliar spray by hand. Problem vegetation near roads, trails, parking lots, utilities |
| Stalker (BASF) Arsenal®, Habitat®, Chopper®, Polaris /Raptor/Eraser/Alligare |
| CAS No: 81510-83-0 |
| 2-[4,5- dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol- 2-yl]-3-pyridinecarboxylic acid |
| Imazapyr is stable, clear, slightly viscous, pale yellow to dark green aqueous liquid |
| Vapor Pressure is very low (0.0000002) and flash point is not relevant. |
| Imazapyr is of relatively low toxicity to mammals and shows no mutagenic or teratogenic potential. It can be an eye and skin irritant, but is not a dermal sensitizer |
| Practically nontoxic to fish, aquatic invertebrates, birds, terrestrial vertebrates |

### Mode of Action

Imazapyr is a non-selective herbicide used for the control of a broad range of weeds including terrestrial annual and perennial grasses and broadleaved herbs, woody species, and riparian and emergent aquatic species. Imazapyr is a pre-emergent and post-emergent bare ground herbicide for control of unwanted vegetation in non-cropland areas and aquatic sites. It will sterilize the soil where it is applied, and nothing will grow for up to 1 year. Imazapyr can also be used in pastures, rangelands and other listed areas. It controls plant growth by preventing the synthesis of branched-chain amino acids. Imazapyr is absorbed quickly through plant tissue and can be taken up by roots. It is translocated in the xylem and phloem to the tissues, where it inhibits the enzyme acetohydroxy acid synthase (AHAS), also known as acetolactate synthase (ALS). ALS catalyzes the production of three branched-chain aliphatic amino acids, valine, leucine, and isoleucine, required for protein synthesis and cell growth. Environmental pH determines its chemical structure, which in turn determines its environmental persistence and mobility. Below pH 5 the adsorption capacity of imazapyr increases and limits its movement in soil. Above pH 5, greater concentrations of imazapyr become negatively charged, fail to bind tightly with soils, and remain available (for plant uptake and/or microbial breakdown). In soils, imazapyr is degraded primarily by microbial metabolism. It is not, however, degraded significantly by photolysis or other chemical reactions (Dickens 1986)

### Environmental Fate and Transport

Imazapyr is slowly degraded by microbial metabolism and can be relatively persistent in soils. It has an average half-life in soils that range from one to five months. At pH above 5, it does not bind strongly with

soil particles and can remain available (for plant uptake) in the environment. In water, imazapyr can be rapidly degraded by photolysis with a half-life averaging two days (USEPA 2005). There have been a few reports from the field of unintended damage to desirable, native plants when imazapyr has either exuded out of the roots of treated plants into the surrounding soil, or when intertwined roots transfer the herbicide to non-target plants (Vizantinopoulos and Lolos 1994). In a laboratory study, the half-life of imazapyr ranged from 69-155 days, but factors affecting degradation rates were difficult to identify because the pH varied with temperature and organic content.

**Human Toxicology**

Human toxicity estimates are extrapolated from animal studies. Imazapyr is of relatively low toxicity to mammals and shows no mutagenic or teratogenic potential. It can be an eye and skin irritant but is not a dermal sensitizer (American Cyanamid 1986; Cyanamid Ltd. 1997). Imazapyr acid is categorized as practically non-toxic to small mammals. No mortality or clinical signs of toxicity were observed in acute oral studies. The acute risk to mammals following either broadcast granular application or spray application is expected to be low because the highest dose-based EECs are 0.03 (broadcast spray) to 0.1 (granular application) of the highest concentration tested in the acute study which produced no mortalities and no clinical signs of toxicity.

Chronic studies indicated no evidence of adverse reproductive effects. The chronic LOC for mammals was not exceeded for any of the studies registered with USEPA. The chronic risk for mammals is low following exposure to imazapyr. There is no evidence that imazapyr is carcinogenic or mutagenic. The USEPA has determined that the risk to humans of dietary and incidental exposure is below the level of concern (USEPA 2006).

**Ecological Toxicology**

There are no reported chronic risks of imazapyr to fish and invertebrates. Fish and invertebrates inhabiting surface waters adjacent to an imazapyr treated field would not be at risk for adverse acute and/or chronic effects on reproduction, growth, or survival when exposed to imazapyr directly or in residues in surface runoff and spray drift as a result of spray application. Risk to benthic organisms is also not likely based on the available toxicity data and because imazapyr is not expected to accumulate in benthic systems. Very Low toxicity to rats (Oral LD50 for rats >5,000 mg/kg), moderate toxicity for rabbits, dermal LD50 >2,000 mg/kg) and low toxicity to fish, LC50 for bluegill sunfish:>100 mg/LC.

Imazapyr is of relatively low toxicity to birds and mammals. The LD50 for rats is > 5,000 mg/kg, and for bobwhite quail and mallard ducks is >2,150 mg/kg. American Cyanamid reports that studies with rats indicate that imazapyr was excreted rapidly in the urine and feces with no residues accumulating in the liver, kidney, muscle, fat, or blood (Tu et al. 2004). Uncertainties remain about the potential toxic effects in animals due to the lack of toxicity data on reptiles and amphibians.

Imazapyr has not been found to cause mutations or birth defects in animals and is classified by the USEPA as a Group E compound, indicating that imazapyr shows no evidence of carcinogenicity. The LC50s for rainbow trout, bluegill sunfish, channel catfish, and the water flea (*Daphnia magna*) are all >100 mg/L. Imazapyr (tradename Habitat®) is registered for use in aquatic areas, including brackish and coastal waters, to control emerged, floating, and riparian/wetland species. A recent study from a tidal estuary in Washington showed that imazapyr, even when supplied at concentrations up to 1600 mg/L, did not affect the osmoregulatory capacity of Chinook salmon smolts. Washington State Department of Agriculture (2003) reported that the 96-hour LC50 for rainbow trout fry to be 77,716 mg/L (ppm). Limited information was found on the effects of imazapyr on other non-target organisms such as soil bacteria and fungi. The manufacturers report that Arsenal® is non-mutagenic to bacteria (American Cyanamid 1986).

### Typical Application Scenarios For Imazapyr/Stalker

For terrestrial applications of imazapyr, the main application method is modeled: directed foliar (backpack); associated risk estimates are shown in Table 9. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure, the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates.

### Table 9. Estimates of Potential Risk synthesized from USEPA data and SERA 2011

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.003, 0.03, 0.01 | SERA 2011 |

Source: SERA 2011.

(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Stalker would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Stalker in excess of USEPA-defined safe levels. There are numerous formulations of imazapyr but most of the toxicity data available is for Arsenal (BASF). The risk estimates are thus based on uses and application techniques of Arsenal.

The risk assessments used to evaluate imazapyr are based on the typical unit application rate of 1 lb a.i./acre, and up to the maximum labeled rate of 1.5 lbs a.i./acre. While imazapyr is an effective terrestrial herbicide, the exposure scenarios used to characterize used for terrestrial and aquatic plants result in a wide range of HQs. The variations are typical of all chemical applications and are impacted by different weather patterns and other site-specific variables.

Using typical exposure and risk estimates associated with typical applications of imazapyr, there is no indication that the applications will pose any substantial risk to humans or other species of animals. The USEPA/OPP classifies imazapyr as practically non-toxic to mammals, birds, honeybees, fish, and aquatic invertebrates. None of the expected (non-accidental) exposures to these groups of animals raise substantial concern.

## Surflan AS CAUTION

## Oryzalin (>38 Products)

| |
|---|
| Preemergence control of both grasses and broadleaved weeds |
| Cut-stump, basal bark, foliar spray by hand |
| Dirimal/EL-119/Rycelan/Ryzelon/Surflan |
| CAS No 19044-88-3 |
| Bright orange, opaque liquid with slight aromatic odor. Biodegrades slowly. |
| 3,5-dinitro-N4, N4-dipropylsulfanilamide |
| Low vapor pressure. Flash point >200F |
| practically nontoxic to birds, small mammals and honeybees |
| moderately toxic to freshwater fish, invertebrates |

### Mode of Action

Oryzalin acts by inhibiting cell division in plants. It is used to control annual grasses, broadleaf weeds, woody shrubs and vines in grapes, berries and orchard crops, including both fruits and nuts. It also is used on residential and commercial/industrial lawns and turf, golf course turf, ornamentals and shade trees, Christmas tree plantations, fencerows/hedgerows, nonagricultural rights-of-way, and uncultivated areas including patios, paths, paved areas and power stations.

### Environmental Fate and Transport

Oryzalin biodegrades slowly with a half-life of approximately two months. It is not mobile under most field conditions and is not volatile. Up to 20 percent of the breakdown products of oryzalin have the potential to leach into the soil but the level of leaching varies according to the physiochemical environment (Elanco 1989).

### Human Toxicology

Human toxicity estimates are extrapolated from animal studies. Oryzalin generally is of moderate acute toxicity but is carcinogenic in animal studies and has been classified as a Group C, possible human carcinogen. Several food-crop uses, including grapes and a variety of fruits and nuts, are registered and allowable and dietary exposure to oryzalin residues in foods is extremely low, as is the cancer risk posed by this herbicide to the general population (SERA 2014).

In acute toxicity studies using laboratory animals, oryzalin is practically non-toxic by the oral route and has been placed in Toxicity Category IV (the lowest of four categories) for this effect. It is of moderate dermal and inhalation toxicity and causes slight eye irritation and has been placed in Toxicity Category III for these effects. No skin sensitization occurred in tests on guinea pigs. In subchronic toxicity studies, oryzalin caused the accumulation of an iron-containing pigment in the kidneys of rats, an increase in the weights of several organs in mice, and blood, bone marrow and liver effects in beagle dogs (OHS 1992).

Oryzalin is carcinogenic in rats, based on an increase in mammary gland tumors in females and skin and thyroid tumors in both sexes. It has been classified as a Group C carcinogen--that is, a possible human carcinogen for which there is limited animal evidence. Another chronic toxicity study using beagle dogs showed effects to the blood, liver, kidneys and thyroid gland. In developmental toxicity studies using rats, oryzalin caused reduced maternal body weight as well as decreased fetal body weights, an increase in runts and bone development effects. In rabbits, it caused reduced maternal food consumption and weight

gain, fetal effects and reduced litter size. Reproduction studies using rats showed increased liver and kidney weights, and decreased food consumption and body weight gain. Oryzalin was not mutagenic in several studies.

### Ecological Toxicology

Oryzalin is moderately toxic to freshwater fish and invertebrates, and practically nontoxic to birds, small mammals and honeybees. Minor risks to birds are posed from acute and dietary exposure to oryzalin. Chronic risks are not posed at single application rates of 4 pounds active ingredient per acre (4 lb ai/A) or less. Oryzalin does not appear to pose a risk to nonendangered freshwater fish (USEPA 1994). However, a Daphnia life-cycle study is needed to determine the chronic risk to freshwater invertebrates. Oryzalin appears to pose a risk to endangered aquatic species in shallow water adjacent to treated areas. Oryzalin is moderately toxic to freshwater fish and invertebrates, and practically nontoxic to birds, small mammals and honeybees (Meister 1992)

### Typical Application Scenarios For Oryzalin/Surflan

For terrestrial applications of oryzalin, the main type of application method would be foliar spray (backpack); associated risk estimates are shown in Table 10. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure, the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates (SERA 2014, 2015).

**Table 10. Estimates of Potential Risk Synthesized from USEPA data and SERA 2014**

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.001, 0.0026, 0.062 | SERA 2015 |

Source: SERA 2014.

(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Surflan would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Surflan in excess of USEPA-defined safe levels.

USEPA has developed risk parameters for oryzalin. The acute RfD for oryzalin is 0.05 mg/kg bw/day and the chronic RfD for oryzalin is 0.14 mg/kg bw/day (USEPA 1994). The RfDs are developed using an uncertainty factor of 100. The HQs for workers based on carcinogenicity are 0.001 (0.00002 to 0.06). These estimates of risk are associated with a single day's 8 hr. exposure, which represents a typical application event. Thus, based on this estimated exposure, an individual would need to apply oryzalin for 1,000 days to reach a cancer risk of 1-in-1-million.

USEPA (1994) estimates an exposure of 0.01 mg/kg 17 bw/day for individuals applying oryzalin by ground broadcast application (no broadcast spraying would occur under the WVFMP). Based on the cancer potency factor of 0.13 (mg/kg bw/day)-1, the risk [Dose x Potency] to individuals would be about

[0.13 (mg/kg bw/day)-19 x 0.01 mg/kg bw/day = 0.0013 or about 1 in 769]. The highest risk listed in the USEPA documents is 2.6x10-4 (USEPA 1994).

# Transline CAUTION

## Clopyralid (>16 Products)

Several retail herbicide products contain the active ingredient clopyralid

| |
|---|
| Used for thistles, knapweeds, locust, kudzu |
| Cut-stump, basal bark, foliar spray by hand |
| Transline/stinger/reclaim/Lontrel/clopyralid MEA |
| CAS No. 57754-85-5 |
| Clopyralid 3,6-dichloroo-2-prridinecarboxylic acid. |
| Liquid red to brown with sweet odor |
| Nonvolatile and highly water soluble. Can be flammable as vapor |
| Very low toxicity to rats, no evidence of mutagenicity, carcinogenicity or reproductive toxicology |
| Low toxicity to fish, birds and aquatic invertebrates |

### Mode of Action

Clopyralid is a selective herbicide used for broadleaf noxious weed control, and it is the active ingredient in Transline. It is structurally similar to aminopyralid, which has an extra amino group, and it is also an auxin hormone mimic, causing abnormal growth that impairs proper nutrient transport throughout the plant. It is highly selective for terrestrial plants and appears to be relatively non-toxic to aquatic plants (SERA 2004).

### Environmental Fate and Transport

Clopyralid is relatively nonvolatile and highly water soluble. It is stable to both hydrolysis and photolysis in aqueous systems but is degraded rapidly (Cox 1998). It is degraded in soil primarily through microbial activity (t ½ = 40 days), and carbon dioxide is the major breakdown product (USDOE 2000). It is very stable under anaerobic conditions. It is mobile and does not bind tightly to soil. Clopyralid is very stable in compost piles, and thus is no longer used for lawn and garden applications in California and Washington.

### Human Toxicology

Human toxicity estimates are extrapolated from animal studies. Clopyralid is listed as a Category III compound for oral, dermal, and inhalation toxicity. The oral and dermal mammalian LD50s are both >5,000 mg/kg, and the mammalian inhalation LC50 is >1.3 mg/L. It is not metabolized extensively; 79-96% of parent clopyralid is excreted in rat urine (t ½ = 3 hr.) (SERA 2004). The No Observable Effect Level (NOEL), which is the highest dose that results in no effect, in dogs is 100 mg/kg/day. Clinical signs of acute clopyralid poisoning include neurotoxicity, manifested as ataxia, tremors, convulsions, and weakness. Chronic studies in rats, mice, and dogs have noted general decreases in body weight and increases in liver and kidney weight, which are commonly observed in chronic toxicity studies and can indicate either an adaptive or toxic response. The USEPA OPP has established an acute RfD of 0.75 mg/kg/day and a chronic RfD of 0.15 mg/kg/day for clopyralid.

The USEPA classifies clopyralid as a Group E human carcinogen (no evidence of carcinogenicity) because chronic studies in rats, mice, and dogs have shown no indication of carcinogenicity. However, technical grade clopyralid contains low levels of hexachlorobenzene (<2.5 ppm), which is classified as a potential human carcinogen (SERA 2004).

Recent panel reviews by the European Food Safety Authority (EFSA 2012) considered the status of clopyralid in Europe to consider the renewal of the registration of clopyralid as an herbicide on winter cereals and grassland. The panel's review of the available risk assessment information did not substantially alter the mammalian and toxicity information. The acute and long-term risk to birds and mammals from oral exposure via residues in food items and contaminated drinking water was assessed as low. No risk assessment for secondary poisoning was triggered based on the low Log Pow (< 3). Numerous recent publications refining the information about clopoyralid were identified but none that would substantially alter the basic information or characterization of the potential effects of clopyralid use by UC Berkeley.

### Ecological Toxicology

Clopyralid is practically non-toxic to slightly toxic to birds. The oral LD50 in mallard duck is >1,645 mg/kg. The dietary LC50 for both pure clopyralid and the monoethanolamine salt of clopyralid is >4,460 ppm in both bobwhite quail and mallard ducks. Clopyralid is also practically non-toxic to fish and aquatic invertebrates (USEPA 2002). The 96-h LC50 in bluegill is 125 mg/L, and the LC50 in rainbow trout is 103 mg/L for technical grade clopyralid. The monoethanolamine salts are even less toxic to fish, with LC50s ranging from 700-1,645 mg a.i./L. There is no indication that clopyralid bioaccumulates in fish. The LC50 in *Daphnia* is 225 mg/L. In a chronic *Daphnia* reproduction study, the NOEL was found to be 23.1 mg a.i./L (SERA 2004). Clopyralid is also practically non-toxic to honeybees; the contact LD50 is >100 µg/bee. Clopyralid residues are highly toxic to non-target broadleaf plants.

### Typical Application Scenarios For Clopyralid/Transline

For terrestrial applications of clopyralid, the main type of application method is directed foliar (backpack); associated risk estimates are shown in Table 11. Several standard exposure rates (mg/kg bw per lb/acre) are used to calculate risk estimates. Because of the sensitivity of each parameter used to estimate exposure the risk estimates generally extend across a large range of values. The most appropriate estimate generally represents a mid-point in the estimates.

**Table 11. Estimates of Potential Risk synthesized from USEPA data and SERA 2004**

Calculated risk estimates include the lower, central, and upper statistical values of the data distribution.

Calculated values are compared to the standard level of concern at 1x10-4 using USEPA risk parameters.

| Application Method | Lower, Central and Upper risk estimates of risk per lb handled (mg/kg bw) | Reference |
|---|---|---|
| Directed foliar | 0.0003, 0.003, 0.01 | SERA 2004 |

Source: SERA 2004. TR 04-43-17-03c Clopyralid Human Health and Ecological Risk Assessment Final Report.
(calculations based on typical applicator exposure in an 8hr day).

Even using the upper bound estimate of exposure, which is very conservative, risks to applicators would be adequately addressed by ensuring proper handling and proper use of PPE. Because Transline would be applied according to label direction during implementation of the WVFMP, members of the general public would not be exposed to Transline in excess of USEPA-defined safe levels.

The USEPA OPP has established an acute RfD of 0.75 mg/kg/day and a chronic RfD of 0.15 mg/kg/day for clopyralid. Regardless of the low likelihood of substantial exposure to applied triclopyr, several highly conservative scenarios can be used to illustrate the potential risks of adverse effects. For terrestrial applications of clopyralid, as with many herbicides, the greatest exposures are actually associated with the acute and longer-term consumption of contaminated fruit and vegetation. This is typical of any pesticide exposure following foliar application. Exposures associated with dermal contact and the consumption of water (except for an accidental spill) are considerably lower.

## Summary and Conclusions of WVFMP Herbicide Evaluations

Each of the herbicides proposed for use under the WVFMP were evaluated for toxicity and/or potential adverse human health and environmental effects; the results are summarized in Table 12. The hazard information, exposure assumptions, and potential toxicity associated with the listed active ingredients have been addressed. This review suggests that minimal to no substantial adverse environmental impacts are expected from herbicide use proposed under the WVFMP. Use of these products within the label restrictions and following regulatory guidance is not expected to result in any significant adverse impacts to human health or the environment.

Overall, the proposed uses of herbicides under the WVFMP should provide adequate and reasonable safe margins because they will be used according to label guidance and more restrictive environmental protection guidance. The herbicides reviewed, and the uses proposed, are considered reasonable with minimal to no potential adverse impacts. However, reports in the media have raised public concerns that should be noted regarding glyphosate. Most of those reports are based on equivocal correlations, not supported by defensible relevant studies illustrating causality. Instead, the primary body of research suggests these herbicides are safe to use according to label directions and restrictions.

## Other Issues Related to Herbicides

### Risks Related to Flammability and Accelerants

The flash point is the lowest temperature at which a liquid will form a vapor that will briefly ignite when exposed to an open flame. The flash point of liquids is one of the most dangerous characteristics of a chemical. The flash point is a general indication of the flammability or combustibility of a liquid. Below the flash point, insufficient vapor is available to support combustion. At some temperature above the flash point, the liquid will produce enough vapor to support combustion (the fire point). The determination of volatility (vapor pressure at which the liquid becomes a gas such as evaporation) is the condition under which a liquid is at an equilibrium as a vapor above its liquid (in a closed container). Vapor pressure and flash point is determined for every registered herbicide and is included in the MSDS.

Some comparisons illustrate the relative flash points of liquids: automotive gasoline, -45F, ethyl alcohol 55F, automotive diesel fuel 100F. Herbicides often contain some of these heavy petroleum constituents but not sufficient to result in a dangerous flash point. Most herbicides have flash points well above 150F and thus are safe to use without concern about flash point or flammability (NCBI 2017). Because the herbicides proposed by the WVFMP have high flash points, flammability during handling is not an issue. The retention of herbicide residue that could impact the flammability of target vegetation varies across plant species and physical conditions. Examples of residue times of several herbicides reported the dissipation rates at < 40 days under mild climatic conditions (Michael and Neary 1993).

**Table 12. Toxicity Summary of Herbicide Active Ingredients**

| Active Ingredient | Mammalian Oral LD50 (mg/kg)A | Mammalian Dermal LD50 (mg/kg)B | Mammalian Inhalation LC50 (mg/L)A | USEPA Toxicity Rating | Carcinogenic | Reproductive or Developmental toxicity | Neurotoxic | Immunotoxic | Endocrine Disruption |
|---|---|---|---|---|---|---|---|---|---|
| Triclopyr Garlon 4 Ultra | >5,000 | >5,000 | >5.79 | Oral, dermal, inhalation (IV) | No | No | No | No | No |
| Glyphosate RoundUp RoundUp Pro | >4,320 (technical); ≥5,000 (salts) | ≥2,000 (tech); ≥5,000 (salts) | ≥4.43 (tech); >1.3 (salts) | Oral, dermal, inhalation (III) | No | No | No | No | In human cell lines at very high doses |
| Isoxaben Snapshot 2.5 | >5,000 | >5,000 | >5.71 | Oral, dermal, inhalation (IV) | No | No | No | No | NA |
| Trifluralin Snapshot 2.5 | >5,000 | >5,000 | >5.71 | Oral, dermal, inhalation (IV) | No | No | No | No | NA |
| Imazapyr Stalker | >5,000 | >2,000 | >1.3 | Oral, dermal, inhalation (IV) | No | No | No | No | No |
| Oryzalin Surflan AS | >5,000 | >2,000 | na | Oral, dermal, inhalation (IV) | No | No | No | No | No |
| Clopyralid Transline | >5,000 | >5,000 | >3.0 | Oral, dermal, inhalation (III) | No (may contain hexachlorobenzene) | No | No | No | No |

Source: Adapted by Infinity Solutions 2020. Toxicity data are derived from respective sections in this document and summarized for the categories used by USEPA and other regulators. Some data represent the most likely values within the typical range of effects in the literature

With the extensive use of herbicides in vegetation management, public concern has increased about the fate of pesticides in fires. Studies conducted on herbicides indicate that hot fires (>500 C) thermally degrade most pesticides. Smoldering fires (<500 C) have the potential to volatilize few herbicides. However, as described above for each herbicide proposed for use, herbicides break down over time, do not persist in the environment, and most post no risk of flammability such that a substantial risk related to fire would be created.

In some instances, the method of vegetation control may include prescribed burning by qualified fire personnel. This method sometimes incorporates chemical accelerants to assure a focused and complete ignition of the targeted vegetation.

The USFS has provided many reports addressing the potential impacts and risks of their use of fire accelerants to ignite prescribed burns. Table 13, Chemicals List, presents the fire accelerants, their chemical components, and the residues expected to remain following combustion. Because accelerants are used only for special focused and monitored uses, the likelihood of unintended adverse impacts is low.

**Table 13. Comparison of Calculated/Estimated Risk Associated with Accelerants**

| Accelerant Used | Estimated HQ Risk | Comment |
|---|---|---|
| Aluminum oxide | 1.92 E-01 | Launcher Pistol |
| Gasoline+MTBE | 1.09 E-02 | Added 9.51E-03 + 1.35E-03 |
| Gasoline + Diesel Fuel | 1.17 E-02 | Mixtures critical |
| Gelled Gasoline +MTBE+aluminum oxide | 1.96 E-02 | Concern about residual coating |
| Gelling agent + Aluminum oxide | 8.71E-03 | Concern about residual coating |

Source: USFS. 2002.

The USFS has compiled an evaluation of the potential impacts to humans and wildlife from use of these chemicals. The compilation of relative "risks" from the use of accelerants is based on calculated exposure/target toxicity values similar to the HQs used in human and wildlife toxicology. Although each of the accelerants listed have been evaluated to generate risk estimates, the estimates are based on extended exposures in the laboratory and therefore are conservative and do not represent the likely effects after a typical application.

The HQs that may result in adverse effects to applicators/handlers are depicted by values nearest to unity. An HQ of 1.0 suggests that the exposure may be of concern (HQ of 1.0 E-0). The calculated estimated risk values provide a comparison of the potential for adverse effects to the applicator. These values are an extension of the hazard values extrapolated to a typical handling scenario. Given that all of the values are below 1.0 there is no substantial risk associated with the proper use of these accelerants.

### Issues Related to the Potential Interactions of Herbicides

#### *Synergism and Antagonism*

Mixing chemicals in some cases can be problematic and the resulting impacts can be characterized as synergistic, antagonistic and/or additive. *Synergism* means an effect or effects arising between two or more active ingredients, or an active ingredient and one or more inert ingredients, that is greater than the sum of their individual effects. *Antagonistic* means the effects are less than the effects of the original chemical. *Additive effects* become the sum of the individual effects of the two chemicals.

Most commercially available herbicides are already a combination of active ingredients and can be safely used if the label recommendations and guidance are followed. Every product available to the public has been evaluated by both federal and private organizations to arrive at the recommended use rates and handling precautions. Over the past several years concern has developed in the public sector that in some cases the combinations of ingredients may cause synergistic effects because most pesticide product labels do not meaningfully limit tank mixtures and timing of applications. For this reason, USEPA has included, where appropriate, consideration of potential synergistic effects of pesticide products during its registration and registration review process (Zhou et al. 2005). Many of the registration reviews now include protective label restrictions to eliminate potential adverse, synergistic impacts (USEPA 2019).

Numerous studies and pesticide evaluations have been supported by the manufacturers and the scientific community to provide clear guidance on the potential synergistic and/or antagonistic effects of application of multiple pesticides on a site (Ma et al. 1992). Simplistic recommendations include extended time allotted between herbicide applications, care in the specific types of vegetation that is treated (many herbicides are toxic to specific types of vegetation) and physical separation often is sufficient to avoid interactions.

Zhang et al. (1995) developed a computer modelled synthetic data set by incorporating results from previously published papers on antagonistic and synergistic herbicide interactions between two herbicides. The comparisons considered herbicides applied as a tank mixture or sequentially, and then analyzed on the basis of various properties of the herbicides and target plants. Generally, interactions between herbicides were antagonistic more frequently than synergistic. This trend held regardless of whether the interacting herbicides were absorbed by the same or different parts of the plant, had the same or different translocating abilities, had the same or different modes of action, and regardless of whether the target plants were annual or perennial plants, or crops or weeds. Antagonistic interactions occurred much more frequently when the target plants were monocot than dicot, and in the Composite, Gramineae, or Leguminosae than in the Chenopodiaceae or Convolvulaceae families (Zhang et al. 1995).

Because herbicide applications proposed under the WVFMP would follow all herbicide label requirements, which take into account potential synergistic effects, the risk of synergism such that adverse effects to human health or the environment would occur are low.

**Issues Related to the Safety of Treated Vegetation to Grazing Animals**

There is no clear way to determine the residual herbicide on target vegetation without actual timed measurements of the plant tissue. As an alternative to actual residue measurements, it is useful to consider the half-life of an herbicide in soil and the time it takes to break down into a non-toxic form. The half-life is the time it takes for 50% of the chemical to degrade or break down. Soil half-lives are only an indication of potential residual because half-life varies substantially with soil type and other conditions. For all soil types, half-lives are affected by pH, temperature, moisture content, sunlight and concentration of active ingredient. Higher temperatures, greater soil moisture, high bacterial activity and high levels of organic matter tend to accelerate degradation; dry and cold conditions tend to lengthen degradation. Dry or drought conditions are the main factor in causing herbicide residues to persist longer than normal.(USEPA 2017).

The majority of residentially sold herbicides are required by law to break down in the soil within 14 days, if not sooner. As an example, the non-selective herbicide glyphosate generally breaks down within days to weeks depending on the specific product (USEPA 2017). Most herbicides are relatively non-toxic to mammals so that a substantial amount of treated vegetation would need to be consumed to approach or exceed the documented toxicity of the herbicide.

## References

## Garlon 4 Ultra (Triclopyr)


California Environmental Protection Agency (EPA). 1986. Summary of Toxicology Data for Triclopyr; California Environmental Protection Agency, Department of Pesticide Regulation, Human Health Assessment Branch: Sacramento, CA, 1986.

———. 1997. Environmental Fate of Triclopyr; California Environmental Protection Agency, Department of Pesticide Regulation, Environmental Monitoring & Pest Management Branch: Sacramento, CA, 1997.

De Roos, A.J., S.H. Zahm, K.P. Cantor et al. 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occu Environ Med* 2003.

National Pesticide Information Center (NPIC) Product Research Online (NPRO). 2018. Triclopyr. National Pesticide Information Center. Corvallis, OR.

Syracuse Environmental Research Associates, Inc. (SERA). 1996. *Triclopyr – Garlon 3A and Garlon 4 Risk Assessment, Final Report, SERA TR 95-22-02-02a*. Report dated March 31, 1996. Prepared under USDA/FS contract by Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

———. 2002. *Neurotoxicity, Immunotoxicity, and Endocrine Disruption with Specific Commentary on Glyphosate, Triclopyr, and Hexazinone: Final Report, SERA TR 01-43-08-04a,* Report dated February 14, 2002. Prepared under USDA Forest Service contract by Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

———. 2003. *Triclopyr - Human Health and Ecological Risk Assessments, Final Report, SERA TR 02-43-13-03b,* Report dated March 15, 2003. Prepared under USDA Forest Service contract by Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

———. 2004. *Clopyralid - Human Health and Ecological Risk Assessment - Final Report*. Prepared for USDA/Forest Service and National Park Service.

———. 2011. *Triclopyr - Human Health and Ecological Risk Assessment, Final Report, SERA TR-052-25-03a*. Report dated May 24, 2011. Prepared under USDA Forest Service contract by Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

———. 2014. *Reassessment of Worker Exposure Rates – FINAL REPORT. SERA TR-056-06-02b*. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

University of California Office of the President (UCOP). 2019. *University of California Herbicide Task Force Update*.

———. 2020. *University of California Herbicide Task Force Report and Recommendations.*

U.S. Forest Service (USFS). 2011. *Triclopyr Human Health and Ecological Risk Assessment*. U.S. Department of Agriculture, Forest Service. Atlanta, GA.

U.S. Environmental Protection Agency (USEPA). 1998a. RED Facts Triclopyr, Office of Prevention, Pesticides, and Toxic Substances (7508C). EPA-738-F-98-007.

———. 1998b. Reregistration Eligibility Decision: Triclopyr; U.S. Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC.

———. 2014. Human Health Assessment Scoping Document in Support of Registration Review for Triclopyr; Triclopyr, Triethylamine Salt (TEA); and Triclopyr, Butoxyethyl Ester (BEE); U.S. Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, U.S. Government Printing Office: Washington, DC.

## Glyphosate (Roundup Pro)

Andreotti, G and S Koutrus, Jonathan N. Hofmann, Dale P Sandler, Jay H. Lubin, Charles F. Lynch, Catherine C Lerro, Anneclaire J. De Roos, Christine G. Parks, Michael C. R. Alavanja, Debra T. Silverman, Laura E Beane Freeman. 2018. Glyphosate use and Cancer Incidence in the Agricultural Hearth Study. *Jour. National Cancer Institute*.

Becerra, X. Case 2:17-cv-02401-WBS-EFB Document 83 Filed 03/26/18. NATIONAL ASSOCIATION OF WHEAT GROWERS ET AL.

Brandli, D., and S. Reinacher. 2012. Herbizide im Urin. *Ithaka Jour* 1,9-12.

De Roos, A.J., S.H. Zahm, K.P. Cantor et al. 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occup. Environ Med* 2003; 60: E11.

DeWayne Johnson v. Monsanto Company. 2016. No. 3:2016cv01244 – Justia/Document 52 (No Date, California 2016).

Gertsberg, D. 2011. Safety Review of Glyphosate Herbicide Faces Tough Critics. http://gmo-journal.com/2011.

Koutros S, Harris SA, Spinelli JJ, Blair A, McLaughlin JR, Zahm SH, Kim S, Albert PS, Kachuri L, Pahwa M, Cantor KP, Weisenburger DD, Pahwa P, Pardo LA, Dosman JA, Demers PA, and Beane Freeman LE. 2019. Non-Hodgkin Lymphoma Risk And Organophosphate and Carbamate Insecticide Use in the North American Pooled Project. *Environ Int.* 2019 Jun;127:199-205.

Mahler, CP. 1992. National Toxicology Program Technical Report on the Toxicity Studies of Glyphosate (CAS No. 1071-83-6) Administered in Dosed Feed To F344/N Rats And B6C3F1 Mice. *J Toxicity Report Series*, 30 Jun 1992

Mannetje,t A, De Roos AJ, Boffetta P, Vermeulen R, Benke G, Fritschi L, Brennan P, Foretova L, Maynadié M, Becker N, Nieters A, Staines A, Campagna M, Chiu B, Clavel J, de Sanjose S, Hartge P, Holly EA, Bracci P, Linet MS, Monnereau A, Orsi L, Purdue MP, Rothman N, Lan Q, Kane E, Seniori Costantini A, Miligi L, Spinelli JJ, Zheng T, Cocco P, Kricker A. 2016. Occupation and risk of non-Hodgkin lymphoma and its subtypes: a pooled analysis from the InterLymph Consortium. *Environ Health Perspect* 124:396-405

Miller, A., Gervais, J.A., Luukinen, B., Buhl, K., Stone, D., 2010. Glyphosate Technical Fact Sheet, in: *National Pesticide Information Center, Oregon State University Extension Services*(Ed.).

Monsanto Company 2017. Glyphosate & Salts of Glyphosate Toxicological and Toxicokinetic Studies. Unpublished study prepared by Monsanto Company. 417p. https://www.sciencedirect.com/science/article/pii/S1383574218300887?mc_cid=23c18e62e7&mc_eid=ff8c3a64ef

National Pesticide Information Center (NPIC). 2019. Glyphosate General Fact Sheet. http://npic.orst.edu/factsheets/glyphogen.html.

Pahwa M, Beane Freeman LE, Spinelli JJ, Blair A, McLaughlin JR, Zahm SH, Cantor KP, Weisenburger, DD, Punam Pahwa PP, Dosman JA, Demers PA, Harris SA. Glyphosate use and associations with non-Hodgkin lymphoma major histological sub-types: findings from the North American Pooled Project. *Scand. J Work Environ Health*. 2019 Nov 1;45(6):600-609.

Portier CJ, Armstrong BK, Baguley BC, Baur X, Belyaev I, Bellé R, et al. 2016. Differences in the carcinogenic evaluation of glyphosate between the international agency for research on cancer (IARC) and the European Food Safety Authority (EFSA). *J Epidemiol Community Health*:jech-2015-207005.

Schuette, J., 1998. *Environmental Fate of Glyphosate*. Environmental Monitoring and Pest Management, Department of Pesticide Regulation.

Siemering, G., 2005. *Aquatics Herbicides: Overview of Usage, Fate and Transport, Potential Environmental Risk, and Future Recommendations for the Sacramento-San Joaquin Delta and Central Valley White Paper for the Interagency Ecological Program*. FEI Contribution 414. San Francisco Estuary Institute, Oakland, CA.

Syracuse Environmental Research Associates, Inc. (SERA). 2011. *Glyphosate. Human Health and Ecological Risk Assessment*. Syracuse Environmental Research Associates, Inc., TR-0052-22-03b.

———. 2014. *Reassessment of Worker Exposure Rates – FINAL REPORT. SERA TR-056-06-02b*. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

Tarazona et al. (2017): Glyphosate toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC. *Arch Toxicol*. 2017 Aug;91(8):2723-2743.

Tarone, RE., 2018. On the International Agency for Research on Cancer classification of glyphosate as a probable human carcinogen. *Eur J Cancer Prevention Jan*; 27(1):82-87.

University of California Office of the President (UCOP). 2019. *University of California Herbicide Task Force Update*.

———. 2020. *University of California Herbicide Task Force Report and Recommendations*.

U.S. District Court Eastern District of Missouri, Case No. 4:17CV01252 AGF (May 25, 2018). https://www.roundupconcentratesettlement.com/content/documents/58. Order%20Granting%20Final%20Approval.pdf USEPA 2014. Enlist-Duo Registration. Dow AgroSciences. USEPA No. 62719-649.

U.S. Environmental Protection Agency (USEPA). 1993. Reregistration eligibility decision (RED) glyphosate, Office of Prevention, Pesticides, and Toxic Substances (7508W). EPA 738-R-93-014.

———. 2009a. Environmental Protection Agency Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened Under the Federal Food, Drug, and Cosmetic Act. *Federal Register* 74:17579-17585.

———. 2009b. Environmental Protection Agency Final List of Initial Pesticide Active Ingredients and Pesticide Inert Ingredients to be Screened Under the Federal Food, Drug, and Cosmetic Act. *Federal Register* 74, 17579-17585.

———. 2014. *Endocrine Disruptor Screening Program Comprehensive Management Plan*. Office of Chemical Safety & Pollution Prevention and Office of Water. USEPA Publication 2014.

———. 2016a. Registration of Enlist Duo. U.S. Environmental Protection Agency. https://www.epa.gov/ingredients-used-pesticide-products/registration-enlist-duo. December 6, 2016.

———. 2017a. Revised glyphosate issue paper: Evaluation of carcinogenic potential.

———. 2017b. *Glyphosate. Draft Human Health Risk Assessment in Support of Registration Review*. Office of Pesticide Programs December12, 2017

Williams GM, Aardema M, Acquavella J, Berry SC, Brusick D, Burns MM, et al. 2016. A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to IARC assessment. *Critical reviews in toxicology* 46:3-20.

Williams, G.M., R. Kroes, and 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). 2009. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2009*. WHO Library Cataloguing-in-Publication Data.

———. 2015. Joint FAO/WHO Meeting on Pesticide Residues JMPR 2015 -Publication Data.

## Snapshot 2.5 TG (isoxaben)

Federal Register. 2018. Isoxaben. Vol. 83, No. 26, Wednesday, February 7, 2018. [EPA–HQ–OPP–2016–0650; FRL–9972–75]

Integrated Risk Information System. (IRIS). 1998 (January 4). Review of Isoxaben-Reevaluation Following the Sept. 1988 Science Advisory Panel Review.

Syracuse Environmental Research Associates, Inc. (SERA). 2011. *SERA TR 00-21-29-02c ISOXABEN Human Health and Ecological Risk Assessment Final Report*.

_____. 2014. *Reassessment of Worker Exposure Rates – Final Report*. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

U.S. Environmental Protection Agency (USEPA). 1988. *FIFRA Science Advisory Panel Executive Summary: A set of Scientific Issues Being Considered by the Agency in Connection with the Peer Review Classification of Isoxaben as a Class C Oncogen.* Stephen L. Johnson, Executive Secretary.

———. 1993. *Wildlife Exposure Factors Handbook*. Volumes 1 and 2. EPA/600/R-93/187a,b. Pagination not continuous. Available NTIS: PB94-174778 and PB94-174779.

———. 1996. Exposure Factors Handbook. Office of Research and Development, National Center for Environmental Assessment, U.S. EPA, Washington, DC. EPA/600/P-95/002Ba-c. Avail. NTIS: PB97-117683, 97-117691, PB97 117709.

## Snapshot 2.5 (trifluralin)

Federal Register. 1982 (February 10). Trifluralin: proposed tolerances. Federal Register 47 (28): 6033-4.

National Center for Biotechnology Information. PubChem Database. 2017. Trifluralin, CID=5569, https://pubchem.ncbi.nlm.nih.gov/compound/Trifluralin.

National Research Council. 1977. *Drinking Water and Health*: Volume 1. Washington, DC: The National Academies Press.

Occupational Health Services. 1991. Mode of carcinogenic action of pesticides inducing thyroid follicular cell tumors in rodents. Occupational Health Services, Inc. 1991. MSDS for Trifluralin. OHS Inc., Secaucus, NJ.

Syracuse Environmental Research Associates, Inc. (SERA). 2007. *Trifluralin Human Health and Ecological Risk Assessment Final Report SERA TR-052-26-03a*. Manlius, NY.

———. 2011. Trifluralin. *Human Health and Ecological Risk Assessment – FINAL REPORT*. SERA TR-052-26-03a. Report dated September 20, 2011. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml. [Std].

———. 2014. *Reassessment of Worker Exposure Rates – FINAL REPORT*. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

Tu, Mandy, C. Hurd, J. M Randall. 2004. Imazapyr. *Weed Control Methods Handbook*. The Nature Conservancy.

U.S. Department of Agriculture, Soil Conservation Service. 1990 (Nov.). SCS/ARS/CES Pesticide Properties Database: Version 2.0 (Summary). USDA - Soil Conservation Service, Syracuse, NY.

U.S. Environmental Protection Agency (USEPA). 1987 (August). *Guidance for the Reregistration of Pesticide Products Containing Trifluralin as the Active Ingredient*. Office of Pesticides and Toxic Substances. US EPA, Washington, DC.

———. 1988. FIFRA Science Advisory Panel Executive Summary: A set of Scientific Issues Being Considered by the Agency in Connection with the Peer Review Classification of Isoxaben as a Class C Oncogen. Stephen L. Johnson, Executive Secretary.

———. 1989 (January). *Health Advisory Summary: Trifluralin*. US EPA, Washington, DC.

WSSA 1989. Herbicide Handbook Committee. *Herbicide Handbook of the Weed Science Society of America*, 6th Ed. WSSA, Champaign, IL.

## Stalker 2.5, Polaris (imazapyr)

American Cyanamid. 1986. *Arsenal Herbicide: Technical Report*. American Cyanamid Agricultural Division.

Cyanamid, Ltd. 1997. Summary of toxicity studies on imazapyr. *Journal of Pesticide Science* 22: 360-364.

Dickens, R. and G. Wehtje. 1986. Mobility and soil solution characteristics of imazapyr (Arsenal) and sulfometuron methyl (Oust) in Alabama soils. *Proc. South. Weed Sci. Soc*. 39:368.

El Azzouzi, M., A. Dahchour, A. Bouhaouss, and M. Ferhat. 1998. Study on the behavior of imazapyr in two Moroccan soils. *Weed Res*. 38:217 -220.

Ma, T., S. Sandhu, Y. Peng, T. Chen, and T. Kim. Synergistic and antagonistic effects on genotoxicity of chemicals commonly found in hazardous waste sites. USEPA, Washington, D.C., EPA/600/j-92/426 (NTIS pb93141257), 1992.

McDowell, R. W., L. M. Condron, B. E. Main, and F. Da Steheib. 1997. Dissipation of imazapyr, flumetsulam and thifensulfuron in soil. *Weed Res*. 37:381 -389.

Miller, P., C. H. Fung, and B. Gingher. 1991. Animal metabolism. Chpt 12 in *The Imidazolinone Herbicides*, D.L. Shaner and S. L. O'Connor, eds. CRC Press. Boca Raton, FL. 290 pgs.

Syracuse Environmental Research Associates, Inc. (SERA). 2011. Imazapyr. *Human Health and Ecological Risk Assessment. Final Report*. SERA TR-052-29-03a

———. 2014. *Reassessment of Worker Exposure Rates – Final Report*. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

Tu, et al. 2004. Imazapyr. *Weed Control Methods Handbook*. The Nature Conservancy.

U.S. Environmental Protection Agency (USEPA). 2005. EFED Ecological Risk Assessment Supporting the Reregistration Eligibility Decision for the Use of the Herbicide, Imazapyr, in Previously Registered Non- Agricultural and Horticultural Setting. OPP OPTS.

———. 2006. Reregistration eligibility decision for imazapyr. List C. Case number 3078. Office of Prevention, Pesticides, and Toxic Substances (7508C). EPA 738-R-06-007/OPP-2005-0495

Vizantinopoulos, S., and P. Lolos. 1994. Persistence and leaching of the herbicide imazapyr in soil. *Bull. Environ. Contam. Toxicol*. 52:404-410.

Washington State Department of Agriculture. 2003.*Ecological Risk Assessment of the Proposed Use of the Herbicide Imazapyr to Control Invasive Cordgrass*. Project No 3000901. ENTRIX, October 2003.

WSSA. 1994. *Herbicide Handbook*. Weed Society of America. Champaign, Illinois. 352 pp.

## Surflan (Oryzalin)

Elanco Chemical Company. 1989. *Summary of Basic Data for Oryzalin Herbicide*. MSDS. Indianapolis, IN: Elanco Products Co.

Meister, R.T. (ed.). 1992. *Farm Chemicals Handbook '92*. Meister Publishing Company, Willoughby, OH.

Occupational Health Services, Inc. 1992 (November 17). MSDS for Oryzalin. OHS Inc., Secaucus, NJ.

Syracuse Environmental Research Associates, Inc. (SERA). *TR-056-13-03-02b Oryzalin: Worksheet Maker Workbook Documentation*. USDSFS Risk Worksheets; Oryzalin

———. 2014. *Reassessment of Worker Exposure Rates – FINAL REPORT*. SERA TR-056-06-02b. November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY.

———. 2015 Oryzalin: Worksheetmaker Workbook Documentation. SERA TR-056-13-03-02b.

U.S. Environmental Protection Agency (USEPA). 1984. Tolerances and exemptions from tolerances for pesticide chemicals in or on raw agricultural commodities; oryzalin. *Federal Register* 49 (226): 45854-5.

———. 1987. *Pesticide Fact Sheet Number 211: Oryzalin*. US EPA, Office of Pesticide Programs, Registration Div., Washington, DC.

———. 1990. Pesticide tolerance for oryzalin. *Federal Register* 55 (119): 25140-1.

———. 1994. *RED: Oryzalin EPA 738-R-94-016*. USEPA, Office of Pesticide Programs, Registration Div., Washington, DC.

———. 2011. *Oryzalin Final Work Plan, Registration Review*. Docket Number EPA-HQ-OPP-2010-0940. May 2011.

Washington State Department of Transportation (WSDOT). 1993. Roadside Vegetation Management: Environmental Impact Statement.

Weed Science Society of America (WSSA) Herbicide Handbook Committee. 1989. *Herbicide Handbook of the Weed Science Society of America*, 6th Ed. WSSA, Champaign, IL.

## Transline (clopyralid)

Cox, C. 1998. Clopyralid - Herbicide Fact Sheet. *Journal of Pesticide Reform.* 18(4).

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues). 2012. Guidance on dermal absorption. *EFSA Journal* 2012; 10(4):2665, 30 pp. https://doi.org/10.2903/j.efsa.2012.2665

Syracuse Environmental Research Associates, Inc. (SERA). 2004. Clopyralid -EXCEL Worksheets for Human Health and Ecological Risk Assessments, SERA EXWS 04-43-17-03c, Version 2.04d, dated December 3, 2004

———. 2004. Clopyralid. *Human Health and Ecological Risk Assessment - Final Report*. SERA TR 04-43-17-03c Clopyralid Human Health and Ecological Risk Assessment Final Report

———. 2014. *Reassessment of Worker Exposure Rates – Final Report*. SERA TR-056-06-02b. Document dated November 17, 2014. Syracuse Environmental Research Associates, Inc., Manlius, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/risk.shtml.

U.S. Department of Energy (USDOE). 2000. Clopyralid Herbicide Fact Sheet, in: Bonneville Power Administration (Ed.).

U.S. Environmental Protection Agency (USEPA). 2002. Clopyralid: Pesticide Tolerance," U.S. Environmental Protection Agency, Federal Register Volume 67, Number 186, September 25, 2002, pages 60155–60159.

## Other Issues Related to Herbicides

Bush, PB., D.G. Neary, and C.K. McMahon. 2000. Fire and pesticides: a review of air quality considerations. Pages 132- 136 in W. Keith Moser and Cynthia E Moser (eds.). Fire and forest ecology: innovative silviculture and vegetation management. Tall Timbers Fire Ecology Conference Proceedings, No. 21. Tall Timbers Research Station, Tallahassee, FL.

Ma, T., S. Sandhu, Y. Peng, T. Chen, and T. Kim. 1992. Synergistic and antagonistic effects on genotoxicity of chemicals commonly found in hazardous waste sites. USEPA, Washington, DC.

Michael, J., and D.G. Neary. 1993. Herbicide dissipation studies in southern forest ecosystems. *Env Tox and Chemistry*.

National Center for Biotechnology Information. PubChem Database. 2017. *Trifluralin*. https://pubchem.ncbi.nlm.nih.gov/compound/Trifluralin.

USFS. 2002. *Residues of Fire Accelerant Chemicals*. Volume II: Literature Search. Prepared by Labat, Inc. Mclean VA.

U.S. Environmental Protection Agency (USEPA). 2017. https://www.epa.gov/caddis-vol2/caddis-volume-2-sources-stressors-responses-herbicides#main-content.

———. 2019. *Pesticides; Interim Process for Evaluating Potential Synergistic Effects of Pesticides During the Registration Process; Notice of Availability and Request for Comments*. EPA-HQ-OPP-2017-043.

Zhang, J, A Hamill and S Weaver. 1995. Antagonism and Synergism Between Herbicides: Trends from Previous Studies. *Seed Technology* (9) No. 1. Jan 1995, pp 86- 90.

Zhou, Y., C. Zhong, I. M. Kennedy, V. J. Leppert, and K. E. Pinkerton. 2003. Oxidative Stress And NFKB Activation In The Lungs Of Rats: A Synergistic Interaction Between Soot And Iron Particles. (R829215). *Toxicology and Applied Pharmacology* 190(2):157-169.