United States
Department of
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Forest Service
Pacific Northwest Region

**Healthy Forests Make
A World of Difference**

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Glyphosate

HERBICIDE INFORMATION PROFILE

This information profile is produced by the USDA Forest Service, Pacific Northwest Region, for employees, forest workers, and the public. It provides information on forest and land management uses, environmental and human health effects, and safety precautions for the herbicide glyphosate and its formulations. A list of definitions is included in Section VIII of this profile. For general information on herbicide use by the Forest Service, refer to the PNW Region Treatment Methods Profile for Herbicides which is available at http:/www.fs.fed.us/pnw/.

The principal sources of information and findings in this profile are the PNW Region FEIS (Final Environmental Impact Statement) for Managing Competing and Unwanted Vegetation (USDA/FS 1988), an updated risk assessment on glyphosate prepared for the Forest Service (SERA 1996 available at http:/www/fs/fed/us/foresthealth /pesticide/safety_data/risk.html) and herbicide and surfactant product labels and Material Safety Data Sheets. Information from other sources is specifically referenced.

The PNW Region periodically publishes a bibliography of recent anecdotal and scientific accounts, and analyzes reported worker health effects. This herbicide information profile is updated from a previous profile prepared in February 1997 and reflects new information from a review of new published literature.

I. BASIC INFORMATION

COMMON NAME: Glyphosate

CHEMICAL NAME: N-(phosphonomethyl) glycine

PRODUCT NAMES: Accord®, Rodeo®, Roundup®, Roundup Pro®, Glypro®, Glypro Plus®.

PESTICIDE CLASSIFICATION: Herbicide

REGISTERED USE STATUS: "General Use"

FORMULATIONS: This profile includes two formulations - Glypro and Glypro Plus - that were not addressed in the previous PNW information profile or the SERA (1996) risk assessment. Information on these formulations is taken from the product labels and Material Safety Data Sheets for the

formulations (Dow AgroSciences 1999a,b, 2000a,b).

All of the formulations contain the isopropylamine salt of glyphosate plus inert ingredients. Inert ingredients are anything added to the product other than the active plant-killing ingredient.

The contents of six glyphosate formulations are listed below:

Accord®
glyphosate (41.5%) and water (58.5%)
Rodeo®
glyphosate (53.8%) and water (46.2%)
Roundup®
glyphosate (41.0%); related organic acids of glyphosate (1.5%); isopropylamine (0.5%); polyethoxylated tallow amine surfactant (15.4%) and water (41.6%)
Roundup Pro®
glyphosate (41%); phosphate ester neutralized ethoxylated tallow amine surfactant (14.5%) and water (44.5%)
Glypro®
glyphosate (58.3%);
inerts ingredients(46.2%)
Glypro Plus®
glyphosate (41.0%);
inerts ingredients(59.0%)

Rodeo®, Accord®, and Glypro® labels require that other chemicals, called surfactants, be added to the herbicide for certain kinds of spray applications. A herbicide + surfactant mixture is similar to a formulation of the herbicide such as Roundup®. Surfactants are not tested as extensively as the active ingredients in herbicide formulations. The available information on six surfactants recommended by Monsanto for use with Accord® or Rodeo® was reviewed by Diamond and Durkin (1997). This profile includes publicly available information on potential effects on the human environment from using these surfactants in Forest Service applications. The surfactants and their manufacturers are:

Accord® herbicide + Entry II® Monsanto

Entry II® surfactant consists of 35.0% ethoxylated tallow amine and 65.0% inert ingredients, which are the same compounds, other than glyphosate, found in Roundup®. The potential health and environmental effects of using Accord® plus Entry II® in Forest Service applications are covered in the information on Roundup®.

Rodeo® herbicide + R-11® Wilbur-Ellis
LI-700® Loveland Industries
Agri-Dex® Helena Chemical
Latron AG-98®-AG Rohm and Haas
Latron AG-98®-N Rohm and Haas

Many surfactants could be used with Rodeo® to comply with label directions. The chemical constituents of these surfactants, and data and evaluations of their effects are presented in this profile where information is available.

Glypro® contains about the same concentration of glyphosate as Rodeo®. As with Rodeo, Glypro® requires the addition of a nonionic surfactant and Glypro® may be applied directly to water for the control of emerged weeds (Dow AgroSciences 1999a). Glypro Plus® appears to be similar to Roundup in that the addition of a surfactant is not recommended (Dow AgroSciences 1999b). While the inert ingredients in Glypro Plus® do not specify that a surfactant is included in the formulation (Dow Agro Sciences 1999b, 2000 b), the product label

does indicate that gastrointestinal irritation may occur if large amounts of freshly sprayed vegetation are consumed. As detailed in SERA (1996), gastrointestinal irritation has been associated with surfactants in Roundup®. Unlike Roundup®, which is much more toxic to aquatic species than Rodeo®, the toxicity of Glypro Plus® is identical to that of Glypro® based on information included in the MSDS's for Glypro® and Glypro Plus® (Dow Agro Sciences 1999a,b).

RESIDUE ASSAY METHODS: The U.S. EPA (EMMI 2000) specifies two analytical methods for glyphosate in water: high performance liquid chromatography (HPLC) and high performance liquid chromatography with a fluorescence detector (HPLCFD). The limits of detection for these two methods are 25 and 6 ppb respectively (EMMI 2000). Somewhat lower detection limits for glyphosate in water, 1.0-4 ppb, are reported for HPLC in the published literature (Oppenhuizen and Cowell, 1991; Mallat and Barcelo 1998). HPLCFD also was used to monitor glyphosate in cereal, with a limit of detection of 500 ppb (Hogendoorn et al. 1999). Ion chromatography also may be used to monitor glyphosate in water; however, the reported limit of detection, 42 ppb is higher than the reported limits for HPLC.

II. HERBICIDE USES

REGISTERED FORESTRY, RANGELAND, RIGHT-OF-WAY USES: The uses for glyphosate include planting site preparation, conifer release, forest nurseries, rights-of-way and facilities maintenance, and noxious weed control. Rodeo® and Glypro® are labeled for control of emerged weeds in fresh or brackish water. Roundup® Pro and Accord® can be used to control or suppress *Bromus* species and Medusahead grasses in industrial, rangeland, and pasture sites in CO, ID, IA, KS, MT, NE, ND, OR, SD, UT, WA, and WY under supplemental labels. An additional supplemental labeling for Accord® specifies the use of broadcast applications for weed control in Christmas tree plantations in WA and OR.

OPERATIONAL DETAILS:

TARGET PLANTS: Glyphosate is a broad-spectrum, non-selective, post-emergence herbicide. Glyphosate is used to control grasses, herbaceous plants, including deep rooted perennial weeds, brush, some broad-leaf trees and shrubs, and some conifers. Glyphosate does not control all broadleaf woody plants. Timing is critical for effectiveness on some broadleaf woody plants and conifers.

MODE OF ACTION. Glyphosate is applied to foliage and moves from its point of contact through the plant to and into the root system. Glyphosate inhibits an enzyme found only in plants that is essential to the production of amino acids, which are the building blocks of plant proteins. The plant, unable to make proteins, stops growing and dies. Glyphosate is metabolized or broken down by some plants, while other plants do not break it down. AMPA (amino-methylphosphonate) is the main break-down product of glyphosate in plants. Glyphosate also inhibits plant cytochrome P-450, an enzyme that is involved in the detoxification of some herbicides (Lamb et al. 1998).

METHOD OF APPLICATION: Aerial spraying, spraying from a truck, backpack or hand-held sprayer; wiper application or sponge bars; ropes or sponge wick

applicators, frill treatment; cut stump treatment; aerial or ground injection spray systems; and controlled droplet application.

USE RATES: The maximum labeled application rate for glyphosate is 8 lbs a.i./acre. The Forest Service does not plan to use glyphosate at the highest labeled application rates. In the PNW, application rates are likely to vary from 0.3 to 4.0 lbs a.i./acre.

SPECIAL PRECAUTIONS: Always read all of the information on the product label before using any pesticide. Read the label for application restrictions.

TIMING OF APPLICATION: Apply after leaves expand fully but before fall color change.

DRIFT CONTROL: Do not allow careless application or spray drift. Do not permit spray or spray drift to contact crops or other desirable plants.

IV. ENVIRONMENTAL FATE

SOIL:

RESIDUAL SOIL ACTIVITY: Because glyphosate is strongly adsorbed to soil, relatively little if any absorption occurs through the roots.

A related chemical, called N-nitroso-glyphosate or NNG, was detected in test soils after applying glyphosate at five times the normal use rate. No studies have found conclusive evidence of NNG production using normal application rates (Khan and Young 1977; Newton et al., 1984).

ADSORPTION: Glyphosate and the surfactant used in Roundup® are both strongly adsorbed by the soil.

PERSISTENCE AND DEGRADATION: Glyphosate remains unchanged in the soil for varying lengths of time, depending on soil texture and organic matter content. The half-life of glyphosate in soil can range from 3 to 249 days. Soil microorganisms break down glyphosate and many can use glyphosate as a sole source of phosphorous (Penaloza-Vazquez et al. 1995). The surfactant in Roundup® has a soil half-life of less than 1 week. Soil microorganisms break down the surfactant.

METABOLITES/DEGRADATION PRODUCTS AND POTENTIAL ENVIRONMENTAL EFFECTS: There are two routes of degradation in bacteria, one involving the formation of AMPA (aminomethylphosphonic acid) and the other the formation of glycine (Dick and Quinn 1995; Gard et al. 1997). The formation of AMPA appears to be most common in bacteria from industrial reactors that degrade glyphosate-containing wastes (Dick and Quinn 1995). The main break-down product of the surfactant used in Roundup® is carbon dioxide.

WATER

SOLUBILITY: Glyphosate dissolves easily in water and has a water solubility of about 12,000 ppm.

POTENTIAL FOR LEACHING INTO GROUNDWATER: The potential for leaching is low. Glyphosate and the

surfactant in Roundup® are strongly adsorbed to soil particles and are not easily released back into water moving through soil. In monitoring studies, neither glyphosate nor AMPA were susceptible to leaching after a forest application in British Columbia (Feng and Thompson 1990). In Newfoundland, glyphosate applications of about 8 lbs a.i./acre led to peak/short-term well water concentrations of 45 ppb. No glyphosate was found in well water at single application rates of 3.6 lbs a.i./acre (Smith et al. 1996). The concentration of 45 ppb is a factor of about 400 less than the U.S. EPA 10-day drinking water criteria of 20 ppm (U.S. EPA 1998). Half-lives of glyphosate in groundwater samples ranged from 60 hours in samples exposed to sunlight to 770 hours for samples stored in the dark (Mallat and Barcelo 1998).

SURFACE WATERS: Tests show that the half-life for glyphosate in water ranges from 35 to 63 days. The surfactant half-life ranges from 21 to 28 days. Studies examined glyphosate and AMPA residues in surface water after forest application in British Columbia with and without no-spray streamside zones. With a no-spray streamside zone, very low concentrations were sometimes found in water and sediment after the first heavy rain. Where glyphosate was sprayed over the stream, higher peak concentrations in water always occurred following heavy rain, up to 3 weeks after application. Glyphosate and AMPA residues peaked later in stream sediments, where they persisted for more than 1 year. These residues were not easily released back into the water (Wan 1989).

AIR:

VOLATILIZATION: Glyphosate does not evaporate easily.

POTENTIAL FOR BY-PRODUCTS FROM BURNING OF TREATED VEGETATION: Major products from burning treated vegetation include a glyphosate polycondensate, phosphorus pentoxide, acetonitrile, carbon dioxide and water. Phosphorous pentoxide forms phosphoric acid in the presence of water. No information is available regarding the toxicological properties of the glyphosate polycondensate. There is no information to suggest that the combustion products of glyphosate would contribute substantially to the toxic effects of the combustion by-products of wood.

IV. ECOLOGICAL EFFECTS

SOIL MICROORGANISMS: Most studies show no adverse effects on soil microorganisms, including soil nitrogen cycling processes (USDA-FS 1984). One study found a significant reduction in nitrogen fixation by bacteria associated with clover that was planted in a sandy soil 120 days after glyphosate was applied. The authors could not conclude whether the reduction was due to direct glyphosate effects on the bacteria, or on plant processes that support nitrogen fixation (Eberbach and Douglas 1983). Monitoring of Roundup® application to British Columbia forest soils found no long-term effects to any soil animals or microorganism populations over 6 months. Some populations were reduced after spraying but recovered within 30 days (Preston and Trofymow 1989). Monitoring of pine seedlings and associated mycorrhizal fungi found no effect on seedling growth or ectomycorrhizal development following field

applications of glyphosate in Ontario, Canada (Chakravarty and Chartapaul 1990).

TERRESTRIAL PLANTS: Non-target plants could be damaged by unintentional application or drift. The extent of drift will depend on the specific conditions under which the glyphosate is applied. The potential hazards of drift are greater for aerial applications, compared with ground applications. The extent of damage will depend on the plant species and time of application. Field studies involving both ground and aerial applications of glyphosate suggest that the effects of drift are likely to be most evident within 50 meters of the application site.

Glyphosate and imazapyr appear to have additive toxicity on black cherry and black elm (Nespeca et al. 1998).

AQUATIC PLANTS: Most species of algae and macrophytes do not appear to be more sensitive than fish or aquatic invertebrates to glyphosate. Recent studies on toxicity to algae (Saenz et al. 1997) are consistent with earlier studies summarized in SERA (1996). The toxicity of glyphosate to *Ankistrodesmus*, a species of freshwater green alga, is pH dependent. In unbuffered water, in which the pH was allowed to drop with increasing concentrations of Rodeo®, the 96-hour EC_{50} was 74 ppm. In buffered water in which the pH was held at 7.0, the 96-hour EC_{50} was 412 ppm (Gardner et al. 1997).

Although Rodeo is registered for use as an aquatic herbicide, it is only effective on aquatic plants with vegetation growing above the water level. Roundup® was not toxic to algal species in British Columbia forest streams at post-spray levels, and appears to act as a source of phosphorus for algal growth where the nutrient is in short supply (Austin et al. 1991).

A recent field study conducted in Washington state found that applications of Rodeo® applied with a nonionic surfactant inhibits the growth of duckweed, an aquatic macrophyte (Gardner and Grue 1996).

AQUATIC ANIMALS: Glyphosate is relatively non-toxic to fish, with 24- to 96-hour LC_{50} values ranging from approximately10 ppm in acidic water (pH ≈6) to >200 ppm in alkaline water.

Glyphosate and its formulations were not tested for long-term effects in aquatic animals. Based on the limited available data, however, there does not appear to be a strong relationship between duration of exposure and toxicity. No effects on aquatic invertebrates or fish has been found in a Washington state field study after the application of Rodeo® applied with a nonionic surfactant (Gardner and Grue 1996).

Because of the addition of a surfactant, Roundup® is substantially more toxic than glyphosate, and the relationship of pH to toxicity is the opposite of that for glyphosate. At a relatively acidic pH, LC_{50} values for Roundup® range from about 6 to about 30 ppm for various species. At an alkaline pH, LC_{50} values approach 1 ppm.

Although the surfactant in Roundup Pro® is chemically similar to POEA in Roundup®, no data are available to assess its actual toxicity to aquatic organisms. The toxicity of Roundup Pro® is similar to that of Roundup®, suggesting that there are no substantial differences in toxicity between the

surfactant in Roundup Pro® and the surfactant in Roundup®.

Abdelghani et al. (1997) reported 96-hour LC_{50} values for Roundup® of 14.5 ppm in channel catfish, 13.0 ppm in bluegill sunfish, and about 64,000 ppm in crawfish. In two species of *Daphnia*, 48-hour EC_{50} values of about 65 ppm were estimated using a formulation of glyphosate that contains a different surfactant - characterized only as a oxide-coco-amide-propyl dimethyl-amine (Alberdi et al. 1996). An additional formulation of glyphosate, Roundup Biactive® is available in Australia (Monsanto Australia Limited 2000). This formulation is less toxic than Roundup® to aquatic species based on bioassays in various species of frogs (Mann and Bidwell 1999) as well as bioassays in carp, trout, and *Daphnia magna* (Nomix-Chipman Ltd 1999).

Monsanto conducted aquatic toxicity studies on three surfactants recommended for use with Rodeo® (McLaren/Hart 1995). Studies for R-11® and LI-700® were reviewed and accepted by California EPA (Lapurga 1996). R-11® would be classified as Moderately Toxic to fish and Slightly Toxic to invertebrates; LI-700® and Agri-Dex® would be classified as Practically Nontoxic to both fish and invertebrates.

species	surfactant	LC50
fish	R-11®	3.8 ppm
	LI-700®	130.0 ppm
	Agri-Dex®	>1000.0 ppm
invertebrates	R-11®	19.0 ppm
	LI-700®	190.0 ppm
	Agri-Dex®s	>1000.0 ppm

Conclusions about the absolute toxicity or the relative toxicity among Rodeo®+surfactant formulations cannot be drawn from these data. The combined toxicity of glyphosate and the surfactant used in Roundup® is lower than would be predicted based on acute toxicity of the two components (i.e., there is an apparently antagonistic rather than synergistic joint action) (Diamond and Durkin 1997).

Glyphosate has a relatively low potential for bioconcentration. In a bioconcentration study using ^{14}C-glyphosate, bioconcentration in carp exposed to levels in water of 5–50 ppb ranged from about 10 after 1 day of exposure to about 40 after 14 days of exposure (Wang et al. 1994). These estimates of bioconcentration, however, are based on total radioactivity rather than the identification of glyphosate residues.

TERRESTRIAL ANIMALS: Standard toxicity bioassays were conducted on several wildlife species, including mammals, birds, and some terrestrial invertebrates. In addition, several field studies were conducted on the effects of glyphosate applications comparable or almost the same as those used by the Forest Service.

Data for a single toxic dose (LD_{50}) classify glyphosate as Practically Nontoxic to tested insects and birds. Data for multiple dietary doses classify glyphosate as no more than Slightly Toxic to birds (US EPA 1993a.).

Data for laboratory mice adequately characterized acute toxicity of glyphosate to seven of nine tested wildlife mammalian and amphibian species; adequacy could not be predicted for two other amphibian species (McComb 1990).

In addition to laboratory bioassays, there are several field studies that assessed the effects of glyphosate on terrestrial organisms

(SERA 1996). These studies indicate that effects on terrestrial mammals will be secondary to effects on vegetation at application rates comparable to or greater than those contemplated by the Forest Service, as demonstrated for moose, various small mammals, rabbits, birds, carabid beetles, and various other invertebrates. In some cases, the effects noted in these studies appeared to be beneficial to the species under study. In most cases, the effects noted were changes in population density that reflected changes in food availability or suitable habitat. No remarkable behavioral effects on rough-skinned newts and Townsend's chipmunks were detected after the administration of sublethal doses of glyphosate followed by release into their natural habitat (McComb et al.1990). Recently published field studies also indicate that applications of glyphosate formations are not likely to have an adverse impact on wildlife populations relative to non-herbicide based vegetation management practices (Duchesne et al. 1999; Leutenschlager et al. 1998).

Very few studies suggest the potential for toxic effects. In a laboratory study in which isopods were exposed to leaf litter at levels equivalent to application rates of 2.1 kg/ha, the effect on litter degradation depended on the tree species. Direct toxic effects—evidenced by increased mortality—could not be ruled out but were not statistically significant (Eijsackers 1992). In a laboratory study, effects on earthworm cultures treated at levels equivalent to application rates of 0.7–2.8 g/ha included decreased growth rates and early mortality (Springett and Gray 1992). The direct relevance of this study is limited, however, because the exposure conditions (i.e., spraying twice weekly on culture dishes) represent field conditions. In mammals, most glyphosate is excreted unchanged in urine and feces. Glyphosate was not broken down in rats given oral doses, and it did not bioaccumulate (Brewster et al. 1991). Glyphosate and its formulations were not tested for chronic toxicity on wildlife species. Testing of glyphosate and its formulations on laboratory mammals is reported in Section V.

THREATENED AND ENDANGERED SPECIES: Glyphosate may be a hazard to endangered plants if it is applied to areas where they live. The U.S. EPA identified 76 species that may be endangered by glyphosate use, including 74 species of plant, one species of toad and one species of beetle.

V. HEALTH EFFECTS TESTING

These data, which are the results of laboratory animal studies, were evaluated by the Forest Service and are used to make inferences relative to potential human health effects.

For glyphosate and its formulations, findings are from studies conducted by the manufacturer. These studies were presented to U.S. EPA in support of product registration. The studies may not be available to the public.

Table 1 summarizes the acute toxicity data on glyphosate, glyphosate formulations, and surfactants The U.S. EPA evaluated the studies on glyphosate and glyphosate formulations during the registration process. For Roundup® formulations, data are from studies supplied by the manufacturer, and they are cited in the Material Safety Data Sheets (MSDS). Because Rodeo® and

Table 1. Acute Toxicity

PRODUCT NAME	ACUTE ORAL TOXICITY[a]	ACUTE DERMAL TOXICITY
Glyphosate	Median lethal dose: 4320 mg/kg Slightly toxic (Category III)	Median lethal dose (males): 5010 mg/kg (females): 794 mg/kg Slightly toxic (Category III)
Roundup® formulation	Median lethal dose: >5000 mg/kg Practically nontoxic (Category III)	Median lethal dose: >5000 mg/kg Practically nontoxic (Category IV)
Roundup Pro® formulation	Median lethal dose: >5000 mg/kg Practically nontoxic (Category IV)	Median lethal dose: >5000 mg/kg Practically nontoxic (Category IV)
Agri-Dex® surfactant	Median lethal dose: >5010 mg/kg Pulmonary aspiration hazard	Median lethal dose: >2020 mg/kg Low toxicity
Entry II® surfactant	No more than moderately toxic	No more than moderately toxic
Latron AG-98™ AG surfactant	Median lethal dose: 2000 mg/kg	Median lethal dose: 3000 mg/kg
Latron AG-98™-N surfactant: Nonylphenoxyplyethoxy ethanol Butyl alcohol	 Median lethal dose: >5000 mg/kg Median lethal dose: 790 mg/kg	 Median lethal dose: >3000 mg/kg Medial lethal dose: 3400 mg/kg
LI-700® surfactant	Not specified	Not specified
R-11® surfactant Isopropyl alcohol	 Median lethal dose: 5840 mg/kg (rabbit)	 Median lethal dose: 13 g/kg
PRODUCT NAME	**PRIMARY SKIN IRRITATION** (tests on rabbits)	**PRIMARY EYE IRRITATION** (tests on rabbits)
Glyphosate	Not an irritant (Category IV)	Mild eye irritant (Category III)
Roundup® formulation	Essentially nonirritating (Category IV)	Slight to moderate irritation (Category II)
Roundup Pro® formulation	Essentially nonirritating (Category IV)	Slightly irritating (Category III)
Agri-Dex® surfactant	Moderate irritation	Mild irritation
Entry II® surfactant	Can be irritating	Severely irritating to corrosive
Latron AG-98™ AG surfactant	Substantial irritation	Severe irritation
Latron AG-98™-N surfactant Nonylphenoxyplyethoxy ethanol Butyl alcohol	 Moderate irritation Moderate irritation	 Severe irritation Severe irritation
LI-700® surfactant	Liquid can cause skin burns	Liquid can cause eye burns Vapors are irritating to the eyes
R-11® surfactant	Mild skin irritation or dermatitis	Mildly irritating to the eyes
PRODUCT NAME	**ACUTE INHALATION** (this requirement was waived for glyphosate by the U.S. EPA)	
Roundup® formulation	4-hour LC_{50}: 2.6 mg/L (rat) Slightly toxic (Category III)	
Roundup Pro® formulation	Median lethal concentration: 4.2 mg/L Practically nontoxic (Category IV)	
[a]Tests in male and female rats, unless otherwise specified.		

Accord® formulations consist of glyphosate and water only, the potential health effects from exposure are predicted to be no greater than those for concentrated glyphosate. Consequently, the health effects data for those formulations are not cited.

For LI-700® surfactant, data are from studies

reviewed by California Department of Pesticide Regulation (Lapurga 1996). Product manufacturers reported the data for the other surfactants in MSDS or technical information sheets.

CHRONIC TOXICITY: These data are based on tests in laboratory animals. U.S. EPA requires these tests only for the active ingredient glyphosate. Section X provides an explanation of how the NOEL (No-observed-effects level) is used.

The Pacific Northwest Region FEIS risk assessment evaluated the quality of the testing that was done for glyphosate up to 1988. Quality consideration for individual studies included: ranges of doses and species that were tested; length of test; identification of the most sensitive effect. In addition, the degree of quantitative agreement among all tests for an effect was considered.

SYSTEMIC TOXICITY: Several subchronic or chronic NOELs are available for glyphosate. These values are important because they are used as the basis for characterizing risks from chronic exposure. The PNW FEIS used a NOEL of 31 mg/kg/day from a 26-month feeding study in rats.

The PNW Region FEIS rated the quality of testing as Marginally Adequate; the dose at which effects are seen in animal studies varies widely.

After repeated skin exposure for 3 weeks to Roundup® formulation at five times the recommended use concentration, severe skin irritation and systemic toxic effects were observed in rabbits. Slight to moderate skin irritation was the only effect observed in rabbits treated with three times the recommended use strength.

CARCINOGENICITY: The PNW Region FEIS rated the quality of testing as Marginally Adequate but assumed that glyphosate could cause cancer and conducted a quantitative cancer risk assessment for glyphosate using a cancer potency estimate of 2.6×10^{-5} $(mg/kg/day)^{-1}$ (PNW FEIS, p. 84). The highest worst-case cancer risk was 4 in 100 million (PNW FEIS, p. 5-39).

The Re-registration Eligibility Decision document on glyphosate (U.S. EPA 1993b, dated September 1993) indicates that glyphosate is classified as Group E: Evidence of non-carcinogenicity for humans. This classification is also indicated in U.S. EPA's most recent publication of tolerances for glyphosate (U.S. EPA 1995).

More recently Gold et al. (1997) reported cancer potency estimates of 5.9×10^{-5} to 4.8×10^{-4} $(mg/kg/day)^{-1}$for glyphosate. These are factors of about 2-20 higher than the potency parameter of 2.6×10^{-5} $(mg/kg/day)^{-1}$ used in the PNW FEIS. The potency parameters provided by Gold et al. (1997) are based on experimental data in which there were no statistically significant increases in tumor rates at any dose level. If the highest cancer potency reported in Gold et al. (1997) were used in the PNW FEIS, the worst-case cancer risk would be about 0.8 in 1 million, very close to the threshold of concern (1 in one million) used by the Forest Service.

Hardell and Erikson (1999a) reported an increased cancer risk of non-Hodgkin lymphoma (NHL) in individuals in Sweden who have a history of exposure to

glyphosate. The increased risk was not statistically significant. Acquavella et al. (1999) have criticized the methodology used by Hardell and Erikson (1999a). As part of the response to this criticism, Hardell and Erikson (1999b) reported that an additional analysis of their data pooled with data from another study demonstrated a statistically significant increase in NHL associated with exposures to glyphosate. Details of the pooled analysis are not provided by Hardell and Erikson (1999b).

These results are of concern to the Forest Service, and the Forest Service requested that the U.S. EPA review these studies (Rubin 2000). The U.S. EPA (Tompkins 2000) replied that:

> *The Office of Pesticides Programs Health Effects Division has reviewed the journal article entitled "A Case-Control Study of Non-Hodgkin Lymphoma and Exposure to Pesticides" and concluded that the study does not change EPA's risk assessment for the currently registered uses of glyphosate.*

REPRODUCTION/DEVELOPMENTAL: The U.S. EPA and the PNW Region FEIS used a NOEL of 10 mg/kg/day, based on a 3-generation feeding study in which kidney effects were observed at 30 mg/kg/day but not at 10 mg/kg/day in rat pups. This is also the study that the U.S. EPA (1998) used as the basis for the chronic RfD of 0.1 mg/kg.

The PNW Region FEIS evaluated the testing as Marginally Adequate for these effects. The U.S. EPA (1998) rated confidence in the RfD as high because the quality of the study used for the RfD as well as the quality of the supporting studies is high .

IMMUNE SYSTEM EFFECTS: The PNW Region FEIS evaluated the testing as Inadequate for these effects. El-Gendy et al. (1998) reported that glyphosate concentrations of about 2.8 ppm may inhibit immune function in fish.

NERVOUS SYSTEM EFFECTS: The PNW Region FEIS evaluated the testing as Inadequate for nervous system effects.

VI. HUMAN HEALTH EFFECTS

FOREST SERVICE EVALUATION OF HUMAN HEALTH RISKS: The Pacific Northwest Region evaluated a range of glyphosate health effects data, including some laboratory studies cited in Section V. Both quantitative (numerical) estimates of toxicity, and the quality of data used to make numerical estimates were evaluated. No new studies indicated a reduced margin of safety that would warrant additional restrictions on the use of glyphosate beyond those specified in the FEIS.

The FEIS Quantitative Risk Assessment predicts the amount of human exposure—both to project workers and to the public—from typical forestry operations and also from a large accidental spill. The Risk Assessment uses this information to assess health risks from typical uses. These risks are compared with U.S. EPA standards of acceptable risk for human health effects. The FEIS risk assessment identifies as "Moderate" or "High" any predicted risks from Forest Service operations that were greater than U.S. EPA standards.

Specific mitigation measures were designed to reduce human exposure from these operations; they are mandatory for every

applicable project on National Forest Lands.

The complete set of risk ratings is provided in Section X.

The quality of the existing data affects the reliability of these risk ratings. The FEIS judged the overall quality of the available data on glyphosate toxicity to be "Marginal." There were studies of adequate quality and results did not vary greatly, but more information would increase reliability. Although new studies may change estimates of health effects, the results are considered moderately reliable. The new information cited in Section V would improve the "quality of information" ratings in those categories.

POTENTIAL FOR HEALTH EFFECTS TO THE PUBLIC: Forest visitors and nearby residents could be exposed to herbicide drift, to vegetation with herbicide residues, and to accidental spraying. They also could eat food or drink water containing herbicide residues.

There are no studies regarding public exposure to forest herbicide applications. Public doses were estimated based on the behavior of the herbicide in the environment. "Routine Application" estimates maximum possible public exposure under normal operating conditions. The "Large Spill" situation models the highest doses that reasonably can be expected to occur. Typical public exposures and risks would be much lower than either situation.

MITIGATING MEASURES TO REDUCE IDENTIFIED RISKS TO THE PUBLIC: "Low" risk of general health effects for all routine projects. "Moderate" risk of reproductive health effects for people who receive multiple exposures to glyphosate from a large (400-acre) aerial application project. "Low" risk for smaller (40-acre) aerial projects, and for all ground-based applications:

> Consider potential for public exposure when designing contact procedures, posting and signing needs in the Herbicide Application Plan.

"Moderate" risk of general health effects, and "High" risk of reproductive effects if exposed to concentrated glyphosate from a large spill:

> Prevent all public contact with accidental spills (emergency spill notification system, restrict public access to spill site).

PROBABILITY OF A WORKER RECEIVING A DOSE THAT AFFECTS GENERAL HEALTH OR REPRODUCTION: Worker exposure and dose are estimated for typical forestry applications. Worker doses do not account for decreased exposure resulting from safety precautions or mitigating measures (like wearing protective clothing).

There are studies that measure actual worker doses of herbicide for some typical forestry applications. Backpack applicators of Roundup® in forest plantations were monitored for the doses they absorbed in actual spray operations (Middendorf 1993). The measured doses for workers averaged 1/1000 the amount that was predicted in the PNW Region FEIS for Routine applications, and 1/67 the amount predicted for a Worst-case application situation. SERA (1996) uses the Middendorf (1993) study for their occupational exposure assessments, which accounts for the differences between the PNW/FEIS assessments compared with those in the SERA (1996) assessment, as

indicated in Section X.

MITIGATING MEASURES TO REDUCE IDENTIFIED RISKS TO WORKERS: The probability of worker exposure to a toxic concentration for general health effects was rated "Low" or "Negligible" for all application methods. The probability of worker exposure to a toxic concentration for reproductive effects was rated "Low" or "Negligible" for aerial and tank truck mixer/loaders; "Moderate" for backpack spray and hack-and-squirt applicators.

In the PNW Region FEIS, Mitigating Measure 13 requires workers applying any herbicide to wear protective clothing. Mitigating Measure 23 requires worker exposure monitoring for all herbicide application projects.

The 1992 Amendment to the ROD requires workers to review this Information Profile before agreeing to apply glyphosate herbicides. The worker may request reassignment without penalty. Additional personal protective equipment will be available at the work site for workers who want to reduce their exposure to the herbicide.

ACUTE TOXICITY (POISONING):

REPORTED EFFECTS: Most incidents of human poisoning involve skin or eye irritation in workers after exposure during mixing, loading or application of glyphosate formulations. Nausea and dizziness also were reported after occupational exposures.

Swallowing the Roundup® formulation caused mouth and throat irritation, pain in the abdomen, vomiting, low blood pressure, reduced urine output, and in some cases, death. These effects have only occurred when the concentrate was accidentally or intentionally swallowed, not as a result of the proper use of Roundup®. The amount swallowed averaged about 100 milliliters (about half a cup).

CHRONIC TOXICITY:
REPORTED EFFECTS: There are no reported cases of long-term health effects in humans after exposure to glyphosate or its formulations.

POTENTIAL FOR ADVERSE HEALTH EFFECTS FROM INERT INGREDIENTS AND SURFACTANTS: The manufacturer identified the inert ingredients in glyphosate formulations to the U.S. EPA and to the general public. Inert ingredients in the Roundup® formulation include water and the surfactant POEA. POEA is a skin irritant and a severe eye irritant in concentrated form (Entry II®). The surfactant compounds are more dilute and less toxic in the Roundup® formulation. The only inert ingredient in Rodeo® or Accord® is water, which is considered nontoxic.

U.S. EPA classified all inerts into one of four categories, called "Lists." List 1 contains chemicals of known toxic concern. List 2 contains chemicals of suspected toxic concern which are high priority for testing. List 4A contains chemicals of minimal concern, and List 4B contains chemicals with sufficient information to conclude that current uses will not adversely affect public health and the environment. All other chemicals were classified on List 3: Inerts of unknown toxicity. The U.S. EPA did not find enough information available on the toxic properties of List 3 chemicals to classify them on Lists 1, 2, or 4.

HEALTH EFFECTS FROM EXPOSURE TO FORMULATED PRODUCTS: Because Accord® and Rodeo® contain water as the only inert ingredient, health effects are assumed to be no greater than those for pure glyphosate. The Roundup® formulation is moderately toxic, and may cause skin irritation and eye irritation. Effects of Roundup® characterize the effects expected for a spray mix of Accord® with Entry® II surfactant. Roundup Pro® appears to be similar in toxic properties to Roundup® except it may be less irritating to the skin and eyes (SERA 1996).

The available data for Rodeo® + surfactant formulations are not adequate to assess their potential for toxic effects. Aquatic and mammalian toxicology data for some of the surfactants is provided in Sections IV, V, VI, and VII of this profile. Nevertheless, these data alone are insufficient for predicting either the toxicity of the formulations, or the potential for various surfactants to affect the toxicity of Rodeo® (Diamond and Durkin 1997).

HEALTH EFFECTS ASSOCIATED WITH CONTAMINANTS: Technical grade glyphosate contains an impurity, N-nitrosoglyphosate, which is sometimes abbreviated as NNG. The U.S. EPA determined that 92% of technical grade glyphosate contains NNG at less than 1 ppm and that this amount is toxicologically insignificant (U.S. EPA 1993a).

1,4-Dioxane, a known cancer causing agent, is a common contaminant of ethoxylated surfactants. U.S. EPA decided that reported trace levels of 1,4-dioxane (0.030%) in the Roundup® formulation were not likely to result in unreasonable adverse health effects. More recently, Monsanto reports that 1,4-dioxane contamination was further reduced to 23 ppm (Monsanto Corp. Undated (b)).

HEALTH EFFECTS ASSOCIATED WITH OTHER FORMULATIONS: Some formulations contain glyphosate mixed with other herbicides such as 2,4-D or dicamba. This profile does not fully describe the potential for health or environmental effects from these formulations containing multiple herbicides. Additional information on properties and potential effects of these formulations will be prepared before they are used in the PNW Region.

SOCIETAL PERCEPTIONS: Public opinion about herbicide use, in general, ranges from a perception that herbicides are completely safe, to a perception that they are very hazardous. A full range of opinions is available in the PNW Region FEIS. This profile provides workers and the general public with information that may be useful in assessing the hazards associated with the use of glyphosate in PNW Region National Forests.

VII. SAFETY PRECAUTIONS

SIGNAL WORDS AND DEFINITIONS:

Roundup®: WARNING - Causes substantial but temporary eye injury. Harmful if swallowed or inhaled.

Rodeo®: CAUTION - Harmful if inhaled.

Accord®: CAUTION - May cause eye irritation.

Agri-Dex®: CAUTION - Mild skin and eye irritant.

Entry II®: DANGER - Causes eye burns. Causes skin irritation. Harmful if

swallowed. May cause allergic skin reaction.

Latron AG-98™-AG: WARNING - Causes severe eye and skin irritation. Vapor harmful if inhaled. Harmful if swallowed.

Latron AG-98™-N: WARNING - Causes severe eye irritation and possible permanent injury. Causes skin irritation. Vapor harmful if inhaled. Harmful if swallowed.

LI-700®: DANGER - Liquid causes skin and eye injury.

R-11®: CAUTION - Causes eye irritation. May cause skin irritation. Harmful if swallowed.

PROTECTIVE PRECAUTIONS FOR WORKERS: Avoid contact with eyes, skin, or clothing. Avoid breathing vapors or spray mist. Wash thoroughly with soap and water after handling.

MEDICAL TREATMENT PROCEDURES (ANTIDOTES): There is no specific antidote for glyphosate; treat symptoms. For exposure to the eyes, flush with plenty of water for at least 15 minutes. Get medical attention. For exposure to skin, flush skin with plenty of water. In case of emergency, call your local poison control center for advice.

HANDLING, STORAGE, AND DISPOSAL: Glyphosate is corrosive to unlined steel and galvanized steel. Do not mix, store, or apply glyphosate in galvanized steel or unlined steel containers of spray tanks. Glyphosate is stable under normal storage conditions for at least 5 years. Wastes should be disposed of in a landfill approved for pesticide disposal or according to federal, state, and local rules. Do not contaminate water, food, animal feeds, or seed by storage.

EMERGENCY (SPILL) HAZARDS AND PROCEDURES: Spills that soak into the ground should be dug up and put into plastic-lined metal drums for disposal. Spills on floors or other hard surfaces should be contained or diked. An absorbent clay should be used to soak up the spill. The contaminated absorbent should be put in plastic-lined metal drums. Drums of contaminated soil should be disposed of in a landfill approved for pesticide disposal or according to federal, state, and local rules. Do not contaminate water, food, animal feeds, or seeds by disposal. In case of a large spill, call CHEMTREK at 1-800-424-9300 for advice.

VIII. DEFINITIONS

Absorption -- The process by which a chemical passes through the body membranes and enters the bloodstream. The main routes by which toxic agents are absorbed are the gastrointestinal tract, lungs, and skin.

Acute toxicity – The amount of a substance as a single dose to cause poisoning in a test animal.

Acute exposure -- A single exposure or multiple exposure occurring within a short time (24 hours or less).

Assay -- A kind of test (noun); to test (verb).

Bioconcentration factor -- The concentration of a compound in an aquatic organism divided by the concentration in the ambient water of the organism.

Broadleaf weed -- A nonwoody dicotyledonous plant with wide bladed leaves designated as a pest species in gardens, farms, or forests.

Carcinogen -- A chemical capable of inducing cancer.

Chronic exposure -- Long-term exposure studies often used to determine the carcinogenic potential of chemicals. These studies are usually performed in rats, mice, or dogs and extend over the average lifetime of the species (for a rat, exposure is 2 years).

Contaminants -- Impurities present in a commercial grade chemical.

Dermal -- Pertaining to the skin.

Drift -- That portion of a sprayed chemical that is moved by wind off a target site.

Emerged – In the context of a herbicide that may be applied to aquatic sites, this word refers to aquatic weeds that extend to or beyond the surface of the water. This is in contrast to weeds that are completely below the surface of the water - i.e., submerged.

Formulation -- A commercial preparation of a chemical including any inerts or contaminants.

Half-life – For compounds that are eliminated by first-order kinetics, the time required for the concentration of the chemical to decrease by one half.

Herbicide -- A chemical used to control, suppress, or kill plants, or to severely interrupt their normal growth processes.

Inerts -- Adjuvants or additives in commercial formulations of glyphosate that are not readily active with the other components of the mixture.

Invertebrate -- An animal that does not have a spine (backbone).

LC_{50} – The concentration of a chemical calculated to kill 50% of test animals.

LD_{50} – The dose of a chemical calculated to kill 50% of test animals.

Leach – To dissolve out by the action of water

Lowest-observed-adverse-effect level (LOAEL) -- The lowest dose of a chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Margin of safety (MOS) -- The ratio between an effect or no effect level in an animal and the estimated human dose.

Metabolite -- A compound formed as a result of the metabolism or biochemical change of another compound.

mg/kg -- A common way of expressing dose: milligram of a toxic agent per kilogram of body weight.

Microorganisms -- A generic term for all organisms consisting only of a single cell, such as bacteria, viruses, and fungi.
Nontarget -- Any plant or animal that a treatment inadvertently or unavoidably harms.

No-observed-adverse-effect level (NOAEL) -- The dose of a chemical at which no statistically or biologically significant increases in frequency or severity of adverse effects were observed between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-observed-effect level (NOEL) -- The dose of a chemical at which no treatment-related effects were observed.

Persistence – The tendency of an applied pesticide to remain in the environment.

pH -- The negative log of the hydrogen ion concentration. A high pH (>7) is alkaline or basic and a low pH (<7) is acidic.

ppb -- An abbreviation for *parts per billion*. Equivalent to µg/L for concentrations in water and to µg/kg for concentrations in soil or other non-aqueous media.

ppm -- An abbreviation for *parts per million*. Equivalent to mg/L for concentrations in water and to mg/kg for concentrations in soil or other non-aqueous media.

Reproductive effects -- Adverse effects on the reproductive system that may result from exposure to a chemical or biological agent.

RfD -- A daily dose that is not expected to cause adverse human health effects over a lifetime of exposure. These values are derived by the U.S. EPA.

Surfactant – In the context of herbicide formulations, a surfactant is a chemical compound that enhances the solubility of the formulation making it easier for the herbicide to penetrate into the plant.

Systemic toxicity -- Effects that require absorption and distribution of a toxic agent to a site distant from its entry point at which point effects are produced. Systemic effects are the obverse of local effects.

Toxicity -- The inherent ability of an agent to affect living organisms adversely.

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X. Toxicity and Risk Categories

ESTIMATES OF HEALTH RISK TO THE PUBLIC AND TO WORKERS FROM FOREST SERVICE OPERATIONS: The FEIS predicts levels of human exposure (dose) for project workers and for the public under typical and worst case conditions, including a large accidental spill. These dose levels are compared with the highest dose level in animal tests that showed no effect (NOEL). This level of exposure is referred to as the Margin of Safety or Margin of Exposure approach. The SERA (1996) risk assessment used a conceptually similar approach in which the estimated level of exposure is divided by some estimate of acceptable exposure. Both the FEIS and the SERA (1996) assessment also express risk qualitatively. In the FEIS, the risk is ranked from "Negligible" to "High" based on the margin between the expected human dose and the highest NOEL "no effect" dose. A "High" risk rating means that the highest NOEL dose is not more than 10 times larger than predicted human dose under the specified conditions. A "Moderate" risk rating means that the highest NOEL dose is between 10 and 100 times larger than the expected human dose.

As illustrated in the following tables, the qualitative expression of risk for both workers and the general public is reasonably consistent between the FEIS and the updated SERA (1996) risk assessments. The PNW Region determined that no new information summarized in this profile or in SERA (1996) would change the public or worker mitigations in the 1988 FEIS, which were based on potential human health risks.

Estimated Health Risks To Project Workers[a].

	Risk Category		
	Typical	Lower	Upper
Directed ground[b]	Moderate */Negligible*	Moderate */Negligible*	High */Moderate*

Broadcast ground spray[c]	Low	Negligible	Moderate
Aerial	Low	Negligible	High */Moderate*

[a] From PNW FEIS and SERA1996. Where risk classifications differ in the two assessments, the classification from SERA (1996) is presented in italics.
[b] Backpack only.
[c] Boomspray.

Estimated Health Risks To The Public[a].

Scenario	Risk Category		
	Typical	Lower	Upper
Accidental Spray[b]	Negligible */Low*	Negligible */Low*	Low
Dermal, vegetation [c]	Negligible	Negligible	Moderate /Negligible
Contamin-ated fruit [d]	Negligible	Negligible	Low
Contamin-ated water [d]	Negligible	Negligible	Low/ *Negligible*
Contamin-ated fish [d]	Negligible	Negligible	Negligible
Accidental spill	Low	Negligible	Moderate

[a] From PNW FEIS and SERA 1996. Where risk classifications differ in the two assessments, the classification from SERA is presented in italics.
[b] PNW is based on spray drift. SERA 1996 assessment is based on direct spray.
[c] PNW based on deposition data. SERA 1996 based on Durkin et al.(1995).
[d] PNW is based on short-term exposures. SERA 1996 assessment is based on longer-term exposures.

Avian (Dietary):

mg/kg	Risk Category
<50	very highly toxic
50-500	highly toxic
501-1000	moderately toxic
1001-5000	slightly toxic
>5000	practically non toxic

ECOTOXICOLOGICAL CATEGORIES

Mammalian (Acute Oral):

mg/kg	Risk Category
<10	very highly toxic
10-50	highly toxic
51-500	moderately toxic
501-2000	slightly toxic
>2000	practically non toxic

Avian (Acute Oral):

mg/kg	Risk Category
<10	very highly toxic
10-50	highly toxic
51-500	moderately toxic
501-2000	slightly toxic
>2000	practically non toxic

Aquatic:	
ppm	**Risk Category**
<0.1	very highly toxic
0.1-1	highly toxic
>1-10	moderately toxic
>10-100	slightly toxic
>100	practically non toxic

TABLES OF CATEGORIES OF TOXICITY

Human Hazards				
		Route of Administration		
Risk Category	**Signal Word**	**Oral (mg/kg)**	**Dermal (mg/kg)**	**Inhalation (mg/kg)**
I	**DANGER -- Poison**	0-50	0-200	0-0.2
II	**WARNING**	>50-500	>200-2000	>0.2-2.0
III	**CAUTION**	>500-5000	>2000-20,000	>2.0-20
IV	**NONE**	>5000	>20,000	>20

	Hazard	
Category	**Eye Irritation**	**Skin Irritation**
I	corrosive: corneal opacity not reversible within 7 days	corrosive
II	corneal opacity reversible within 7 days; irritation persisting for 7 days	severe irritation at 72 hours
III	no corneal opacity; irritation reversible within 7 days	moderate irritation at 72 hours
IV	no irritation	mild or slight irritation at 72 hours

Category of Quality of Health Effects Data	
Inadequate:	Inadequate information available for evaluating toxicity. There were too few studies of sufficient quality to yield useful or reliable information.
Marginal-Inadequate:	Some useful information exists for evaluating toxicity. There were studies of marginal quality that provided useful information, but studies were inconsistent and some contained flaws. It is likely that new studies would change estimates of health effects.
Marginal:	Marginal but useful information available for evaluating toxicity. There were studies of adequate quality, and results did not vary greatly, but more information would increase reliability. Although new studies may change estimates of health effects, the results are considered moderately reliable.
Adequate:	Adequate information is available. Studies are of sufficient quality and quantity that estimates of human health are considered reliable. New studies are unlikely to change estimates of health effects.