Exposure of Hand Applicators to Glyphosate in Forest Settings, 1995

May 17, 1999

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Study Dates

Study Initiation	July 1, 1995
Field Monitoring Start	July 12, 1995
Lab Sample Analysis Start	July 24, 1995
Field Monitoring Completion	July 13, 1995
Lab Sample Analysis Completion	November 2, 1995
Study Completion	May 17, 1999

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Approved by: [original signed by J. Sanders] ______________
John Sanders, Branch Chief Date

[original signed by D. Bakke] ______________
Dave Bakke, Pesticide Use Specialist, Region 5, USDA Forest Service Date

[original signed by F. Schneider] ______________
Frank Schneider, Associate Environmental Research Scientist, Study Director Date

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QUALITY ASSURANCE STATEMENT: Project Number 9502

The Forest Service glyphosate worker exposure study was audited at the following intervals:

Audit Date	Phase	Quality Assurance Auditor	Study Director Notified	Management Notified
06/20/95	Protocol	D. Meinders	06/20/95	06/20/95
07/10/95*	Field Monitoring	D. Meinders	07/25/95	07/25/95
08/02/95	Laboratory - Sample Receipt	M. Dostal	08/24/95	08/24/95
08/16/96	Laboratory - Extraction	M. Dostal	09/25/96	09/25/96
09/21/95	Laboratory - Analysis	M. Dostal	09/27/95	09/29/95
01/16/96**	Laboratory - Raw Data	M. Dostal	02/09/96	02/09/96
12/05/97	Raw Data - Report Audit	L. Quagliaroli	12/05/97	12/05/97
03/16/99	Final Report	J. Sanborn	03/16/99	03/16/99

[original signed by J.R. Sanborn] ________
James R Sanborn, Ph.D., Acting Quality Assurance Officer Date

*This audit occurred during monitoring of triclopyr exposure with exposure monitoring continuing for three more days in the exact same manner. Days one and two were used for the dermal exposure monitoring of triclopyr and days three and four were used for this glyphosate exposure study.
**Laboratory raw data audit available from North Coast Laboratories (NCL). Copy of NCL return form showing receipt of raw data audit (QA\MICHELLE\GLPAUDFM) signed by study director/study management not available.

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STUDY COMPLIANCE STATEMENT

Based on the information supplied to me by North Coast Laboratory, LTD. (Certification of GLP) concerning the laboratory analyses of glyphosate, I hereby confirm that all aspects of the worker exposure monitoring portion of this study, Project 9303, were conducted in compliance with the U. S. Environmental Protection Agency, Good Laboratory Practice standards (GLP, 40 CFR 160), with the following exceptions:

The test substance characterization was not documented before its use in the study as required in 40 CFR 160.105(a).

Supplemental and support data such as weather data were not collected in compliance with GLP.

Not all Quality Assurance SOPs were in effect and other required SOPS may not have been in place at the time of study conduct

Protocol and SOP deviations were documented and can be found in Appendix 1.

[original signed by F. Schneider]______________ ______________

Frank Schneider, Date

Associate Environmental Research Scientist

Study Director

Worker Health and Safety Branch

EXPOSURE OF HAND APPLICATORS TO GLYPHOSATE IN FOREST SETTINGS, 1995

EXECUTIVE SUMMARY

Objectives The study objective was to estimate dermal and inhalation exposure of workers who apply glyphosate to National Forest lands. Study estimates were compared to the Forest Service Environmental Impact Statement (EIS) estimates, which were developed using surrogate data.

Background The United States Department of Agriculture (USDA) Forest Service is responsible for managing over 20 million acres of Forest Service land in the Pacific Southwest Region (Region 5). Vegetation management, including mechanical, manual, thermal, biological and chemical means, is necessary to control competing plant species and achieve timber yield objectives. The Forest Service EIS presents the hazard, exposure and risk analyses of the thirteen herbicides used in Region 5. These earlier exposure estimates use animal toxicity data and surrogate data from worker exposure studies with liquid formulations of 2,4-D and 2,4,5-T applied by backpack sprayer, and from estimates of risk based on a range of potential exposure scenarios. In the EIS, realistic, conservative and worst case worker exposures were estimated using the 50^{th}, 95^{th} and 99^{th} percentiles, respectively, of the observed distribution of the 2,4-D and 2,4,5-T worker exposure data. The EIS requires that site-specific worker exposure monitoring evaluate at least 10% of the Region's herbicide application projects annually. In 1995, the Forest Service contracted with the California Environmental Protection Agency, Department of Pesticide Regulation (Cal/EPA, DPR), Worker Health and Safety Branch (WH&S), to conduct the requisite exposure monitoring of workers handling and applying glyphosate.

Methods Monitoring was conducted over two study days. The study evaluated the dermal and inhalation exposure of 10 applicators each day. Applicators used backpack sprayers to apply dilute glyphosate. Dermal exposure monitoring was conducted using long-sleeved cotton T-shirts and knee-length socks, which were worn next to the skin for the duration of the workday. Dermal exposures to the hand and face/neck regions were evaluated by wiping these regions at intervals throughout the workday. Personal air pumps drew air through glass fiber filters to measure glyphosate aerosols. Estimated absorbed dosages (EAD), with standard deviations where appropriate, were calculated for the crew and compared to Forest Service model estimates. EAD calculations were also made using a more recent glyphosate-specific dermal absorption study[14]. WH&S collected additional samples and data to verify the concentration of the test substance, provide quality control and assurance, and to document various study parameters such as the time spent handling glyphosate, amount of glyphosate applied each day, acreage treated, etc.

Major Findings Using the glyphosate specific dermal absorption of 3.7%, EAD averaged 0.021 $\pm$ 0.016 mg/kg and exceeded the conservative exposure scenarios only once and was never above the worst case scenario. Exposures were below the realistic estimate for 80% of the workers. Inhalation exposure was almost non-existent accounting for less than 0.2% of the worker's exposure. Overall exposure varied by seven-fold over the two-day study period. Exposure to the arms and torso accounted for 43% of the dermal exposure while hand, leg and face/neck exposure accounted for 30%, 22% and 5%, respectively. Workers on day one applied more glyphosate and had significantly greater exposure than on day 2 ($p < 0.05$). The worker exposures ranged from 2.3 to 11.9 mg/hr.

A multigenerational rat reproduction study was used to obtain the 10 mg/kg/day NOEL in the EIS[1] because of an increase in focal tubular dilation of the kidney at 30 mg/kg/day. "This effect is now considered spurious rather than glyphosate related because the effect was not observed in a two generation rat reproduction study at dose levels up to 1500 mg/kg/day, the highest dose tested."[15] At the time of the EIS, animal studies were classified as having inadequate animal evidence of carcinogenic potential. With the completion of a repeat rat chronic feeding carcinogenicity study, the reviewers classified glyphosate as showing "evidence of noncarcinogenicty in humans, based upon lack of convincing carcinogenicity evidence in adequate studies in two animal species."[15]. Our study estimated margins of exposure (MOE) for workers handling and applying glyphosate to be 1483 for systemic effects and 478 for reproductive effects. This MOE was estimated using the pesticide-specific data from dermal absorption studies of glyphosate.

Portions of this report were taken verbatim from Spencer, Exposure of Hand Applicators to Granular Hexazinone in Forest Settings, 1993 - 1995. 1997

INTRODUCTION

The USDA Forest Service is responsible for managing over 20 million acres of National Forest Service land in the Pacific Southwest Region (Region 5), of which 30% (6.5 million acres) produces commercial wood products. The Region currently sells between 1.5 and 2 billion board feet of timber each year. Reforestation activities are conducted to reestablish trees and promote stand growth to maintain a continuous supply of timber. Vegetation management is critical to successful reforestation, as control of competing plant species is necessary to achieve timber yield objectives in the Region. Various methods are used to control competition, including mechanical, manual, thermal, biological and chemical means. In their 1988 Environmental Impact Statement (EIS)[1] the Forest Service evaluated the potential health, environmental, economic and social effects of the vegetation management practices used in their reforestation program. Of the various alternatives, herbicide treatments are often the most effective and efficient methods for controlling competing vegetation.

Glyphosate, formulated as the product, Accord® is typically mixed with triclopyr (3,5,6-trichloro-2-pyridinyloxyacetic acid) butoxyethyl ester and applied during the spring to summer months when the target species have emerged. Glyphosate is a non-selective herbicide used extensively to control woody plants, annuals and perennial weeds in reforestation areas and for selective weed control in conifers. The herbicides are applied from a pressurized backpack-sprayer equipped with a hand-held spray gun. The applicators walk through a defined area spraying the foliage of unwanted vegetation.

The Forest Service EIS presents the hazard, exposure and risk analyses of the thirteen herbicides used in Region 5[1]. Human exposure data for herbicide use in forest conditions are limited, the exposure estimates in the EIS relied on extrapolations from animal toxicity data and worker exposure studies with liquid formulations of 2,4-D and 2,4,5-T applied by backpack sprayer, and estimates of risk based on a range of potential exposure scenarios. Realistic, conservative and worst case worker exposures were estimated using the 50th, 95th and 99th percentiles, respectively, of the observed distribution of the 2,4-D and 2,4,5-T worker exposure data. The Forest Service desires to both determine the health effects of herbicides used in their program and to develop techniques and equipment to reduce worker exposures. To accomplish these objectives, the EIS requires that site-specific worker exposure monitoring evaluate at least 10% of the Region’s herbicide application projects annually.

In 1995, the Forest Service contracted with Cal/EPA, DPR, WH&S, to evaluate the dermal and inhalation exposure of workers applying glyphosate using backpack sprayers. In 1994, glyphosate was the third most widely applied chemical in California with more than 136,000 applications taking place and ranked sixth in the amount of material applied at over 3.7 million pounds[2]. The study was conducted in accordance with US EPA, Good Laboratory Practice Standards 40 CFR 160 (GLP)[3] and both DPR and Forest Service regulations. This study evaluated the dermal and inhalation exposure of 10 applicators over 2 study days (20 worker-days). Toxicity endpoints and exposure data referenced in this document were contained in the Forest Service EIS[1]. Estimates of dermal exposure, inhalation exposure and absorbed dose were calculated according to WH&S guidelines[4,5] and compared to EIS[1] estimates for the three exposure scenarios. Dermal exposure monitoring was conducted using long-sleeved cotton T-shirts and knee-length socks, which were worn next to the skin for the duration of the workday. Hand and face/neck dermal exposures were evaluated by using wipes on these regions at intervals throughout the workday. Personal air pumps drew air through a 37-mm diameter glass fiber filter to measure breathing zone concentrations of glyphosate.

An average of 50,000 acres, representing less than 1% of the Region's timber-producing acreage, are treated with herbicides each year[1]. The Forest Service uses herbicides only after evaluating all treatment alternatives and demonstrating their use is essential to achieving project objectives. Herbicides could be applied up to three times during a forest stand rotation of 50 to 150 years: once if needed to prepare the site for planting, and up to two more times to control competing vegetation. Site preparation treatments can be applied from spring through fall. Trees are generally about two years old when planted. Release treatments are made in the first one to seven years post-planting and when competing vegetation is growing. These release treatments free a tree or group of trees from competition by eliminating growth surrounding it.

Materials and Methods

The Forest Service contracted with private applicators to conduct herbicide treatments. Forest Service staff were present at each site to ensure that contract obligations were met. Crews were male and Spanish speaking. The spray crew had ten workers and several baggers. For each plot treated the entire crew began the day by placing plastic bags over the timber species. Then most of the crew switches to spraying while some bag all day. Once spraying is complete the entire crew removes bags. During the day if the applicators catch up with the baggers some or all of the applicators will switch back to bagging. The bags are collected before moving to the next area and reused continuously throughout the day. The applicators load and spray at their own pace rather than working as a group. A dye is added to the spray mix so applicators can gauge their spray swath by the adjacent dyed swath and avoid overlapping each other's application. One worker functioned as the crew leader, carrying water in a sprayer to wash off any mix accidentally applied to timber species. The Forest Service checked spray coverage by measuring off one fiftieth-acre, approximately nine trees, and verifies 90% coverage for each quadrant.

The 300-gallon batch tank was equipped with a 1000-foot hose and trigger nozzle. The system was under pressure so workers are not required to return to the batch tank location to refill their sprayer. It takes about 15 to 20 minutes to make up one batch. The batch tank was filled with water to about two-thirds of the required mix. Measured chemicals were poured in and the mix was topped off to the necessary amount to complete the operation. Glyphosate, [N-(phosphonomethyl)glycine, in the form of its isopropylamine salt] EPA # 524-326, trade name Accord® formulated at 41.5 % active ingredient (4 lb./gallon U.S., 480 g/L equivalent to 3 lb./gallon U.S., 356 g/L of the acid glyphosate) was applied at the rate of 0.25 gallons Accord® per acre (1lb. active ingredient).

Ten workers were monitored for two days of loading and applying glyphosate. They also assisted in placing and removing the plastic bags over seedlings before and after spraying. Applications were conducted using Solo 3.5-gallon backpack sprayers equipped with a 30-inch wand, number 4 flat fan nozzle, (regulator set to 1) and 20 inch pressure pumping bar using up to 15 pounds per square inch. Workers loaded their sprayers by placing the sprayer on the ground, unscrewing the 5 inch cap, inserting the nozzle from the batch tank and filling the tanks by gravity feed or pressure feed system with trigger nozzle. When using the pressure feed system sprayers can be loaded through a hose 1000 feet away from the batch tank. Label clothing requirements are long sleeve shirt, long pants, and shoes plus socks. The work crews wore clean coveralls each day over their own clothing. The coveralls are commercially laundered cotton/polyester or disposable TYVEK®. Coveralls are frequently unzipped partially or totally because the workers become very warm due to the physical nature of the work having to move up and down hillsides. Latex or knit gloves are worn on the hand holding the spray wand or on both hands. Workers also wear hard hats, leather boots, socks and jeans.

The Committee on Human Research, University of California, San Francisco, approved the worker exposure monitoring proposal (number H7420-11293-01)[6]. Department staff read and explained the purpose, procedures, and worker role in the study. The workers were informed they could withdraw from the study at any time and were read the Experimental Subjects Bill of Rights. Questions were solicited and answered prior to seeking voluntary cooperation from the workers. Workers willing to participate in the study then provided signed informed consent. This information was presented in Spanish. No attempt was made to alter the normal clothing worn, personal protective equipment used or work habits of the workers prior to or during exposure monitoring. Prior to initiation of monitoring, the following information was recorded for each worker: sex, height, weight, experience, pesticide exposure the past week. Each worker was assigned an identification number. Notes on each worker for number of loads and the elapsed time to load along with time to apply each load was recorded each day. Observations on clothing worn, personal protective equipment and any circumstances that have the potential to affect the workers' exposure, like spills, bare-handed handling of equipment, and tears in gloves, were recorded.

Inhalation Exposure to glyphosate aerosol was measured by a 37-mm glass fiber filter, type AE (1 µm pore size, SKC number 225-7), backed with a support pad[7]. The filter was housed in a plastic cassette (SKC number 225-2) and sealed with self-sealing bands (SKC number 225-25-01). It was attached via vinyl tubing to a personal air pump (MSA Fixt-Flo, Model S or Model TD), clipped to a webbed belt. The cassette was secured in the worker's collar region and worn for the duration of the workday. Initial pump flow was set at 2 L/min using a Kurz® mass flow meter[8]. Study personnel monitored pump performance throughout the day and replaced pumps as necessary. The sampling matrix was not replaced. Initial and final flow rates and elapsed time were recorded for each pump. At the end of the workday, study staff removed the cassettes from the sampling train, capped the ends and stored each cassette in a separate one-quart Ziploc® bag. All bagged samples were then double-bagged in a one-gallon Ziploc® bag. Samples were stored in insulated coolers on dry ice.

Dermal exposure to the arms and torso of workers was measured using long sleeved, 100% cotton white T-shirts. White knee-length socks (80% cotton/20% polyester) were use to measure residues on the lower leg and foot regions. The socks were also used to estimate exposure to the thigh regions. Clothing dosimetry was worn under the work clothing. Clothing dosimetry permits a direct measurement of dermal exposure to the covered regions without the necessity for extrapolation of patch residues to body surface area[5,9]. At the end of the sampling period, the T-shirt and socks were placed in separate labeled track seal bags, then double bagged. Exposure to the hands and face/neck area was measured by wiping each area with a 100% cotton cloth 6″ x 8″ in size, cut from diapers. The cloth wipes were soaked in a 10:1 solution of water and 0.05% sodium dioctyl sulfosuccinate. Two wipes for each region were collected at break, at any time the worker wished to wash these areas, and at the end of the workday. All dermal sampling media were pre-washed twice in hot water before use. Wipes for each region were combined as one sample for each worker each day. Wipe samples were placed in one-pint canning jars capped with aluminum foil and sealed with standard canning lids and rings. Dermal sample collection at the end of the study day was conducted in the following order starting with hand wipes, face/neck wipes, removal of the T-shirt and removal of the socks. All samples were stored in insulated coolers with dry ice.

The test substance sample of the formulated product Accord®, was collected from the one lot number used for the two study days. A 25-mL sample was collected into a 250-mL jar, capped, labeled, sealed in a track seal bag and stored in a separate cooler with dry ice. Tank mix samples were also collected for each batch load on each study day. An aliquot of at least 100 mL was taken from each batch mixed and two one mL aliquots sub-sampled, then stored immediately on dry ice. This method allowed for the complete extraction of the aliquot and avoided possible problems with settling of the mix, phase changes and hydrolysis.

Field fortifications and blanks accompanied each field shipment for each sampling medium. The purpose of the blanks was to assess handling and shipping conditions, and detect cross-contamination between samples. Dermal matrix blanks were prepared at the end of each study day. The blank for the loaded filter cassette was attached to an air pump via vinyl tubing, the pump was turned on and run the entire study day at 2 liters per minute. Field fortifications served as indicators of the stability of the active ingredient during shipping and storage before extraction and analysis. Three samples of each exposure matrix were spiked each study day with standards prepared from the formulated product. T-shirts, socks and wipes (four per sample) were spiked at 250 μg per sample, the filter cassette was spiked at 5 μg. The dermal dosimetry media were allowed to air dry in the field approximately one hour before storing. All fortifications took place in the back of a truck with shell, at least 50 yards from the application. The spiked filter cassette was handled in the same manner as the blank and allowed to run for the duration of the study period. Filter cassettes with pumps were placed in individual plastic totes in the back of a vehicle to avoid contamination because of the frequent moving to other application sites during the day. The field blanks and fortifications were labeled and stored in the same manner as the exposure samples, on dry ice. Field spikes were extracted with exposure samples using the same methodology and thus used to evaluate storage stability.

Analytical methodology was validated in the lab prior to usage on field samples. Validation was performed on the cotton wipes, T-shirts, socks and AE glass fiber filters. Method validation was conducted according to laboratory standard operating procedures. The fortification levels for glyphosate were 3 replicates at 50 μg /sample, 250 μg /sample and 500 μg /sample for the wipes (four wipes per replicate), T-shirts and socks. Glyphosate method validation for glass fiber filters consisted of 2 replicates performed at 5 μg /sample and 10 μg /sample per filter. Data from the validation study indicated acceptable recoveries for the analyte and matrices. Recoveries were within acceptable limits with average percentages shown in Table 1.

Table 1. Mean percent analytical recoveries for glyphosate acid.

Wipes (4/spl) (n=3)			T-shirts (n=3)			Socks (n=3)			Air filters (n=3)	
LOD	5x LOD	10x LOD	LOD	5x LOD	10x LOD	LOD	5x LOD	10x LOD	LOD	2x LOD
104	108	106	102	105	103	88	95	95	75	79

Glyphosate acid was extracted from all matrices with 0.02 M phosphoric acid. It was analyzed by a high pressure liquid chromatograph and equipped with an o-phthaladehyde post-column reactor and detected with a fluorescence detector with excitation wavelength at 340 and emission at 455 nanometers. Glyphosate was separated using an Alltech 4.6 mm ID X 250 mm glyphosate column with a retention time of approximately 9 minutes. Chromatograms report μg of analyte as glyphosate acid/sample and the calculation is accomplished by the data system. Raw data sheets provided all pertinent calculations for the final results.

<u>Site and workday</u>

Site elevation was about 6000 feet. Terrain varied from moderate to steep slopes. Morning temperatures ranged from 44 - 50 °F and afternoon temperatures were between 72 to 82 °F. The area treated was 450 acres with timber species of Ponderosa, Jeffrey, Sugar pine, White and Douglas fir. The trees planted in 1995, were planted at three trees per 17 foot center and average 450 trees per acre. The timber species were bagged with small plastic produce bags before treatment and bags were removed after treatment. The target species were ceanothus, deerbrush, lupine, and manzanita. Two consecutive days were monitored on the twelfth and thirteenth of July 1995. The first study day was eight hours and 55 minutes beginning at 0655 hours and ending at 1550 hours. The second day began at 0720 hours and was a shorter workday of six hours and 50 minutes ending at 1410 hours. Approximately 32 acres were treated the first day using 800 gallons of tank mix made up in two 300 gallon batch loads and one 200 gallon load (25 gallons/acre batch mix). Twenty-eight acres were treated on the second day, again with three batch loads, with the third load containing 100 gallons. Twenty-four and 21 pounds of glyphosate acid were used for study days one and two, respectively. Of ten total subjects six had one year or less of experience. The crew had been spraying glyphosate and triclopyr on July 10 and 11, subsequent to two days' off. Table 2 reports the workers' heights, weights and years of experience.

Table 2. Study participant information

Worker	Height (cm)	Weight (kg)	Years experience
1	173	85	4
2	178	75	1
3	168	64	1
4	175	77	1
5	183	79	1
6	173	75	1
7	168	61	2
8	168	75	2
9	168	73	3
10	170	58	1

Data Analysis

Field staff recorded the time of loading and application including the time the application began and when it ended. Load times were of very short duration averaging less than 40 seconds. While every load was documented for each worker, some load times were missed due to their brevity. The time to spray one load was 8-10 minutes. The time it took to go to and from the load location were recorded as part of the spray time. The length of the lunch break was recorded. The time the crew spent bagging trees, removing bags, waiting for a new batch load, and putting on and removing study samples was recorded as “other”. Field staff also noted the types of work clothing and PPE worn by each worker, and, as necessary, the time when each worker removed outer clothing as well as any unusual exposure incidents, such as handling herbicide with bare hands, spills of herbicide, etc.

Each sample result was entered into a relational database[10]. Data were analyzed by queries, reports and exporting to a spreadsheet[11]. Individual dermal exposures (mg glyphosate acid x 1.348 correction factor for glyphosate salt) were calculated by summing face/neck wipe residues, hand wipe residues, T-shirt residues and leg exposure (as calculated below). No adjustments were made for workers wearing two pair of socks, or workers with coveralls partially or totally unzipped or torn. While all workers unzipped their coveralls at least partially, we did not attempt to quantify the increased exposure due to a partially open coverall. Hourly exposures (mg glyphosate salt) were calculated by dividing each worker’s dermal exposure by the time each worker spent loading and applying each day. Amount of glyphosate handled per worker was calculated from the number of loads each worker completed relative to the total daily amount applied.

Skin residues: Exposure to the face, neck and hands was evaluated directly by the skin wipes. Upper body exposure (arms and torso): Since T-shirts were considered covered by the coveralls, the dosimetry shirt was assumed to perform as a skin surrogate. Thus, T-shirt residues were considered dermal residues in exposure calculations. Only worker number one wore the coveralls tied at the waist all day, and thus no clothing over the dosimetry shirt. Leg exposure: The study socks captured the glyphosate residues that the workers’ own socks would otherwise have collected. Ten percent of the sock residues were assumed to penetrate the sock to the skin

of the lower legs and feet and be available for dermal absorption[4]. The leg was assumed to receive uniform glyphosate deposition. Thus the thighs (3663 cm2), whose surface area is similar to lower leg and foot surface area (3711 cm2), were assumed to receive exposure equal to the unadjusted sock exposure[4]. No adjustment for clothing penetration was required for thigh exposure, since the thigh, unlike the foot region, was covered by only the pants and coveralls and was not protected by an additional layer of clothing such as a sock. The socks thus performed as skin surrogates for thigh exposure. Leg exposure was equal to the sum of thigh exposure (represented by sock residues) and lower leg exposure (represented by 10% of sock residues), or, a total of 1.1 times the sock residues.
Potential Inhalation Exposure (PIE, mg), Inhalation Exposure (IE, mg) (6) PIE was calculated by adjusting filter residues for pump flow, elapsed time and a 26.7 L/min breathing rate[12].

$$\text{PIE mg glyphosate salt} = \frac{(\text{glyphosate acid } \mu\text{g} \times 1.348 \text{ correction factor for glyphosate salt}) \times (26.7 \text{ breathing rate}) \times (\text{minutes})}{\text{Liters collected}}$$

Inhalation exposure (IE, mg) was calculated by adjusting PIE for 50% uptake and 100% absorption[4]. No adjustments were necessary to the sample results for field recoveries.

Dermal Dose, Estimated Absorbed Dosage (mg/kg) were calculated, using each worker's weight (kg). The Forest Service EIS[1] calculations assumed 10% dermal absorption (dermal penetration). Daily and group means were calculated for dermal exposure and estimate of dosage. The dosage was calculated as 10% of dermal exposure (mg) plus inhalation exposure (mg) divided by body weight in (kg). Additional estimates were made at 3.7% dermal absorption using a review[13] of a glyphosate-specific dermal absorption study conducted in rhesus monkey[14].

Comparisons with Forest Service Models The Forest Service EIS models used the 50th, 95th, and 99th percentiles of exposure estimates from 2,4-D and 2,4,5-T applicator exposure studies to generate estimates of dosage for realistic, conservative and worst case exposures, respectively, to the 13 herbicides used in their spray program. By defining exposures in this manner, the statistics establish the probability of those exposures occurring, i.e., a worst case exposure would be likely to occur 1% of the time. Study data were compared to EIS estimates (mg/kg/day) for workers applying glyphosate by backpack sprayer. The Forest Service model assumed a body weight of 70 kg; the monitoring study used actual worker weights to calculate estimated dosage in mg/kg/day for each worker. The realistic and conservative models assumed glyphosate was applied at 2.75 lb./acre; the worst case model assumed a 5.0 lb./acre application rate. Model estimates were normalized to the observed one pound application rate.

Margins of Exposure (MOE)[1] Glyphosate is classified by US EPA as a Group E carcinogen (evidence of noncarcinogenicity for humans[15]). The EIS hazard analysis, developed from a review of laboratory studies, indicated glyphosate is classified as slightly toxic in rats (LD_{50} = 4320 mg/kg) and has a dermal LD_{50} greater than 5000 mg/kg in rabbits for the formulated product and glyphosate. The EIS established no observable effect levels (NOEL) of 31 mg/kg/day for chronic systemic toxicity (rat) and 10 mg/kg/day for reproductive effects (rat). To evaluate the risks of general systemic and reproductive/teratogenic effects for human exposures, the Forest Service computed a reference dosage by dividing the animal NOEL by an uncertainty factor of 100. Thus, according to the EIS, human exposures (absorbed dosages) below 0.1 mg/kg/day (reproductive) and 0.30 mg/kg/day (systemic) are not expected to carry an excess risk of adverse health effects.

MOE provide indices of relative safety in evaluating human exposures compared to animal NOELs. The MOE is normally calculated by dividing the NOEL of a specified animal toxicity endpoint by a known or estimated absorbed dosage for human exposures. An MOE of less than 100 is usually considered a threshold of concern and indicates the possibility of toxic effects; the lower the MOE, the greater the possibility of these effects occurring. The Forest Service MOE for systemic and chronic effects taken from Table F-54 of the EIS[1] were:

	realistic	conservative	worst
reproductive	125	65	28
chronic	389	201	877

The realistic and conservative estimates used a 2.75 lb./acre application rate while the worst case assumed a 5 lb./acre application rate. The following equations show calculation of the MOE for the Forest Service estimate for systemic effects using the baseline dose of 1 lb./acre, from Table F29[1] and the study MOE. The one pound rate was also the study application rate.

Forest Service MOE = NOEL/EIS $EAD_{realistic}$ (Estimated Absorbed Dosage)

344 = 10 mg/kg/day)/(0.029 mg/kg/day[1]

0.029 mg/kg/day is, also the study application rate)

Study MOE = (10 mg/kg/day)/(0.055 mg/kg/day*) = 181

*Mean EAD for two study days.

Statistical and Graphical Analyses were performed using Microsoft® Excel spreadsheet. Microsoft® Access , Relational Database Management System for Windows contain the raw data, tables, queries and reports.

Results

Table 3 presents daily totals for the time spent applying. The estimated time for loading and the amount of glyphosate sprayed are also given for each worker. The workday also included the time spent bagging trees, getting from one spray area to another by walking or driving and collecting dermal exposure samples. In addition to periodic bagging and bag removal throughout the day all workers usually bagged trees at the beginning of the day and may assist removing them at the end of the day.

Dermal exposure (DE), PIE and IE are reported in Table 4 for each worker and study day. The DE for each body region is also provided. During the monitoring, workers were observed with torn coveralls, wiping up small spills while not wearing gloves, and adjusting nozzles on their sprayers. No adjustments were made to the data because of these occurrences. The higher exposure for the hands of worker seven found on day one was likely the result of wiping up a spill with his gloved hand and his periodic removal of gloves during the day while loading and applying. This probably led to higher exposure to the hands when handling the equipment or contacting the outside of his gloves. In contrast, hand exposure to workers five and six was one tenth of worker seven because they did not remove their gloves to perform other tasks, even though they were observed wiping up spills or adjusting nozzles with gloved hands. Another factor affecting hand exposure is the workers may wear the same pair of gloves for more than one workday. High levels found on some workers' socks could not be explained from the field notes and observations. For example, workers four, eight and ten wore two pair of socks but worker ten had one of the highest sock residues for day 1. On the second day, worker ten wore only one pair of socks and the residues are about one-twentieth those of the previous day. The higher day one exposure may have been due to a moment of accidental exposure that was not observed, for example the worker pulling up his socks with a gloved hand. For the shirt data, worker one tied his coveralls at the waist on both study days and had the highest exposure for day one and one of the highest levels for day two. Other workers had their coveralls partially unzipped or unzipped to waist and no clear distinctions in shirt residue levels were seen. Overall exposure varied by seven-fold over the two-day study period. The upper body accounted for 43% of the dermal exposure while the hand, leg and face/neck areas accounted for 30%, 22% and 5%, respectively. PIE accounted for less than 0.2% of the worker exposure. Since workday length differed substantially for day one and two, dermal and inhalation exposure results are normalized to mg/hour showing a range of 1.6 to 8.8 mg/hr. Workers on day one applied more glyphosate and had significantly greater exposure than on day 2 ($p \geq 0.05$) based on group means.

Table 3. Total time spent for each study applying and loading including total glyphosate handled.

	Day 1 times (hr:mn)				Day 2 times (hr:mn)			
Worker	apply[a]	load[b]	N loads	lbs. applied[c]	apply[a]	load[b]	N loads	lbs. applied[c]
1	3:59	0:17	25	2.63	3:17	0:18	21	2.21
2	3:38	0:15	23	2.42	3:12	0:15	21	2.21
3	3:56	0:16	24	2.52	3:18	0:14	21	2.21
4	3:58	0:15	25	2.63	3:23	0:15	21	2.21
5	3:58	0:16	25	2.63	3:21	0:12	20	2.10
6	4:32	0:16	28	2.94	3:28	0:12	22	2.31
7	3:48	0:16	24	2.52	3:46	0:13	19	2.00
8	3:58	0:17	26	2.73	3:14	0:17	21	2.21
9	4:36	0:19	28	2.94	3:09	0:15	20	2.10
10	4:00	0:14	24	2.52	3:17	0:12	19	2.00

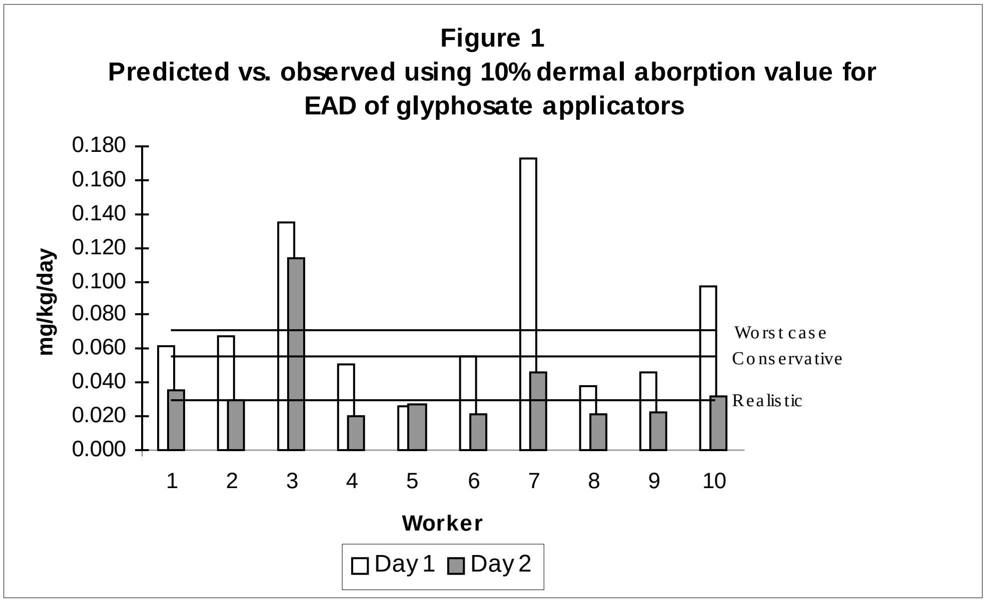
[a] Apply includes only time spent spraying and no other workday activities.
[b] The load time is calculated from the sum of all recorded load times plus the average load time for missing load time data for each worker for the specific study day. Due to the short length of time it took to load not all load times were recorded for each worker.
[c] Pounds applied is a calculation from the number of loads sprayed multiplied by the lbs. a.i./gal in a full backpack sprayer.
N = number of loads

Table 4. Dermal and inhalation exposure (mg glyphosate salt[a]) by worker and day.

Day	Worker	Hands	Face/Neck	Upper body	Legs/feet[b]	DE[c]	PIE[d]	IE[e]	Sum DE+IE	mg/hr[f]
1	1	5.16	1.20	43.25	2.46	52.06	0.131	0.065	52.13	5.85
2		2.19	0.40	25.60	1.35	29.54	0.151	0.076	29.61	4.33
1	2	6.19	2.10	11.05	30.57	49.91	0.133	0.066	49.97	5.60
2		4.18	1.20	10.94	5.76	22.08	0.113	0.057	22.13	3.24
1	3	32.87	5.10	14.88	32.03	88.57	0.103	0.051	88.62	9.94
2		7.65	1.50	34.14	28.63	71.91	0.120	0.060	71.97	10.53
1	4	8.51	1.80	28.16	0.57	39.04	0.083	0.041	39.08	4.38
2		2.72	0.90	10.61	0.70	14.93	0.155	0.078	15.00	2.20
1	5	10.71	2.10	6.47	0.90	20.17	0.108	0.054	20.23	2.27
2		5.72	1.70	12.66	1.22	21.29	0.074	0.037	21.33	3.12
1	6	20.46	2.10	15.78	2.68	24.66	0.078	0.039	24.70	2.77
2		3.87	0.80	9.86	1.04	15.57	0.083	0.042	15.61	2.28
1	7	78.76	4.80	18.81	3.24	105.60	0.121	0.061	105.66	11.85
2		8.69	1.70	13.62	3.67	27.68	0.114	0.057	27.73	4.06
1	8	15.13	3.00	8.19	1.56	27.88	0.076	0.038	27.92	3.13
2		1.91	0.80	11.81	0.72	15.24	0.108	0.054	15.29	2.24
1	9	5.40	1.30	15.73	10.91	33.34	0.097	0.049	33.39	3.74
2		3.57	1.00	5.95	4.61	15.14	0.274	0.137	15.27	2.24
1	10	8.42	1.70	17.59	28.09	55.80	0.112	0.056	55.86	6.26
2		4.22	0.74	11.42	1.46	17.70	0.132	0.066	17.77	2.60
		Summary statistics for day 1								
	Mean	19.16	2.52	17.99	11.30	50.97	0.10	0.05	51.02	5.72
	SD	22.64	1.38	10.74	13.41	26.23	0.02	0.01	26.24	2.94
	Median	9.61	2.10	15.76	2.96	45.46	0.11	0.05	45.52	5.10
	Min	5.16	1.20	6.47	0.57	20.17	0.08	0.04	20.23	2.27
	Max	78.76	5.10	43.25	32.03	105.60	0.13	0.07	105.66	11.85
		Summary statistics for day 2								
	Mean	4.47	1.07	14.66	4.91	25.12	0.13	0.07	25.19	3.69
	SD	2.25	0.44	8.51	8.52	17.27	0.06	0.03	17.27	2.53
	Median	4.02	0.95	11.62	1.40	19.57	0.12	0.06	19.62	2.87
	Min	1.91	0.40	5.95	0.70	14.93	0.07	0.04	15.00	2.20
	Max	8.69	1.70	34.14	28.63	71.91	0.27	0.14	71.97	10.53
		Summary statistics for two days combined								
	Mean	11.82	1.80	16.33	8.11	38.05	0.12	0.06	38.11	4.70
	SD	17.38	1.24	9.59	11.42	25.36	0.04	0.02	25.36	2.87
	Median	5.96	1.60	13.14	2.57	28.71	0.11	0.05	28.77	3.90
	Min	1.91	0.40	5.95	0.57	14.93	0.07	0.04	15.00	2.20
	Max	78.76	5.10	43.25	32.03	105.60	0.27	0.14	105.66	11.85

[a] mg glyphosate salt = glyphosate acid result (found in Appendix 2) multiplied by 1.348
[b] Legs/feet = (sock result multiplied by 1.348) times a factor of 1.1 for clothing penetration[4].
[c] DE =dermal exposure (hands + face/neck + upper body + legs/feet)
[d] PIE = potential inhalation exposure (filter residues adjusted for pump flow, elapsed time and a 26.7 L/min breathing rate[12], see Appendix 5).
[e] IE = Inhalation exposure (adjusted PIE for 50% uptake and 100% absorption[4]).
[f] mg/hr = DE+IE/length of entire workday, 8.9 and 6.8 hours for days one and two.

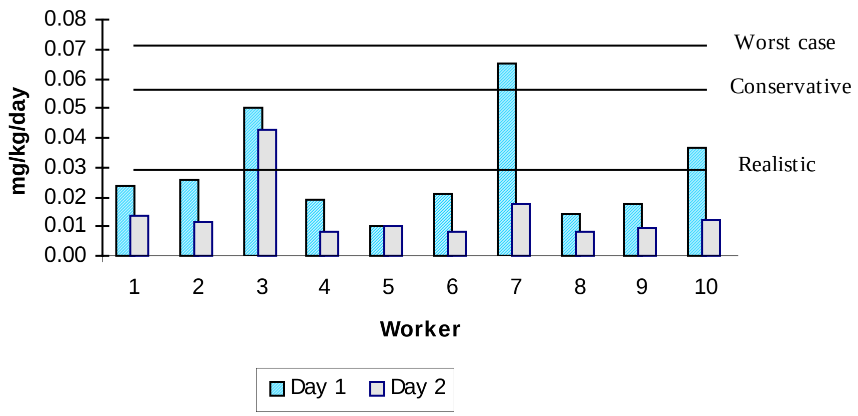
Figure 1 shows both the EAD for all workers by day (normalized to observed application rate) and for the EIS realistic, conservative and worst case predicted exposure scenarios. The EAD averaged 0.056 ± 0.042 mg/kg at 10% dermal absorption and was almost twice the predicted EIS realistic estimate. When the means for each day were calculated separately the day one mean was 0.075 ± 0.047 mg/kg and 0.037± 0.028 mg/kg for day two. Conservative and worst case daily dosage scenarios from the EIS document are 0.056 mg/kg and 0.071 mg/kg, respectively, normalized to the one pound per acre observed application rate. The overall mean and the average of each day are below the EIS conservative and worst case model estimates.



Thongsinthusak, (1996) reviewed a glyphosate dermal absorption study conducted on rhesus monkeys (Wester, et al., 1991[14]) and recommended the average dermal absorption value of 3.7% for use in estimating absorbed dosage for glyphosate exposure[13]. Using this glyphosate-specific dermal absorption value, Figure 2 presents both the predicted and observed EAD for the three EIS exposure scenarios, adjusted for the 3.7% dermal absorption reported in the above study. Exposures are below the realistic estimate for 80% of the workers and average 0.021 ± 0.016 mg/kg and never exceed the worst case scenario.

Test substance and tank mix recovery data are reported in Appendix 3. Sample recovery for the one lot of Accord® used in the study was 98.3 %. Recoveries averaged 104% ± 6% for the six tank mix samples analyzed for the two study days. Recovery of glyphosate from the field fortification standard was 98.2%.

Figure 2
Predicted vs. observed using 3.7% dermal absorption value for EAD of glyphosate applicators



<u>Results of field fortification recoveries</u> are reported in Table 5. Blank samples of each matrix were prepared each study day. All showed non-detected levels of glyphosate acid except for one T-shirt blank from the first study day that showed 14 µg for the sample. Recoveries of laboratory fortifications were above 90%. The 5 µg air filter fortifications averaged 4.97 ± 0.2 µg. The 250 µg fortifications for the three dermal matrices averaged 244 ± 25 µg, 233 ± 19 µg and 253 ± 9 µg for socks, T-shirts and wipes, respectively. The results showed neither contamination nor storage stability losses. All raw data for Table 5 can be found in Appendix 4.

Table 5. Glyphosate field spikes

Matrix	Recovery	Count	Mean	SD
Air filter	100%	6	5	0.4
Socks	104%	6	260	29.6
T-Shirts	94%	6	235	15.5
Wipes	99%	6	248	8.3

Discussion

Dermal exposure was the primary route of worker contact to glyphosate. Past studies[16] have shown the hands to be the primary dermal component of exposure ranging from 23-49%. In this study the hands accounted for 30% of the average exposure, within the range previously reported. Hand exposures for the workers varied by 40-fold over the two study days. While some of this variation is likely due to differences in the length of study day, observations showed one worker frequently not wearing gloves while another worker wore latex gloves over knit gloves or only latex gloves. Use or non-use of gloves can easily account for large variations in hand exposure. A previous study[16] also showed face/neck exposure accounted for one-third of overall exposure as opposed to an average of one-twentieth of the exposure found in our study. Much of the previous data was extrapolated from patches on the chest and back rather than being measured directly. Fenske (1990)[17] found that torso patches did not consistently predict head exposure compared to direct measurements, which varied with work activity and type of application. In our study the face and neck residues were measured directly using the wipes. The torso region, (arms, wrists, back and front from the hip to the super-sternal notch) measured by the T-shirts, was the greatest area of exposure.

No adjustment was made for the exposed portion of the shirt when the coveralls were partially unzipped. Clothing penetration adjustments[4] were made for only the lower leg and foot areas and assumed 10% of the sock residues were available for dermal absorption. Workers normally wear socks and heavy work boots and the pesticide would have to penetrate the boots and socks before coming into contact with the skin. Sock residues were used to extrapolate exposure to the thighs where the worker was protected by his pants and coveralls. The sock thus represents the pesticide that would have reached the workers skin, as it is similarly covered by two clothing layers.

Inhalation exposure was almost non-existent when compared to the dermal exposure measurements. This is primarily due to the use of backpack sprayers operating at low pressures and nozzles that do not allow for atomization of the droplets. This larger droplet size causes the material to fall out of the air rapidly and glyphosate is not volatile (vapor pressure of $<7.5 \times 10^{-8}$ mm Hg at 25° C[18]).

EAD was calculated using 10% dermal absorption, the same value used in the Forest Service EIS exposure models. In conducting exposure assessments, DPR uses dermal absorption data from animals[4] when available. In the case of glyphosate, the animal model[14] was used to calculate an EAD as shown in Figure 2.

For our study, the amount of glyphosate applied is not a useful indication of potential exposure levels ($R^2 <0.04$ for EAD on lbs. applied), even though there was a significant difference in exposure between the two study days. This is probably due to the small difference in pounds applied each day compared to the much greater variability in exposure among workers each day. Exposure databases such as the "Pesticide Handlers Exposure Database" (PHED)[19] require observed exposures to be normalized to a variable, preferably total lb. a.i. handled, before using the model to generate exposure assessments. A backpack applicator moving up and down difficult terrain in the forest is considered more active than a ground applicator operating equipment at an even speed over smooth terrain and is in closer contact with both the spray mix and treated plants. The pesticide exposure to a backpack applicator can be greatly influenced by small unobserved spills, light drift, falls in a treated area or brushing against treated plants.

In reviewing two studies conducted on applicators using backpack sprayers, potential exposures ranged from 9 mg/hr for an applicator spraying parathion[20] on bush tomatoes to 84 mg/hr for a sprayer using 2,4-D in a grassland setting[21]. The second study measured potential dermal exposure from the residues on the coveralls and hands. Using a 10% clothing penetration factor for the second study, the result of 8.4 mg/hr would be in line with the 9 mg/hr cited from the first study. These two studies would then be at the high end of the mg/hr range reported in our study (median of 2.9 mg/hr). Harris (1992)[22] studied homeowners applying 2,4-D. Only three of eleven homeowners showed detectable residues of 2,4-D in urine and in two cases contamination occurred when volunteers worked without gloves during the study. For the third individual, they calculated an absorbed dose of 0.0005 mg/kg/day. This homeowner applied 37.5 grams of 2,4-D or about a thirtieth of what the workers applied during the longer day in our study. Using thirty as a multiplier, the exposure estimate would be 0.015 mg/kg/day. These studies suggest that the range of applicator exposures found in our study are similar to those found by other investigators.

In a glyphosate study[23] of conifer nursery workers spraying seedlings, the dermal exposures ranged from 0.16 - 1.75 mg/hr. One worker had a dermal exposure of 6.0 mg/hr but he mixed and poured for all other applicators. The investigators used 22.9 percent clothing penetration to normalize the data. The workers applied the material using a cylindrical protective shield acting as a spray chamber to avoid drift. The smaller size of the plants and use of the shield probably accounts for the low dermal exposures found. The urinary sampling yielded no positive results. In a study conducted in Finland,[24] five workers doing brush saw spraying were monitored. The investigators collected breathing zone samples, urine samples and conducted clinical exams before and after exposure. Air sampling results ranged from none detected to 15.7 $\mu g/m^3$ and is similar to those in our study (5.0 - 25 $\mu g/m^3$). One urinary sample had detectable glyphosate (0.85 µmol/L). Findings in the medical exam pre- and post-exposure did not differ.

MOE were determined in the EIS[1] using application rates of 2.75 lb./ac for the realistic and conservative estimates and 5 lb./ac for the worst case scenario. The application rate in our study was 1 lb./ac. This lower application rate would increase the MOE for all scenarios reported in the EIS[1] Table F-54 to above 100. Table 6 shows both the predicted MOE for each scenario normalized to the 1 lb.. application rate and the study MOE. The table uses the EIS[1] NOELs of 31 mg/kg for systemic effects and 10 mg/kg for reproductive effects. The MOE for 10% and 3.7% dermal absorption factors are also shown. Using these NOELs, the MOE is well above 100 for systemic and reproductive effects at an application rate of 1 lb. a.i./ac.

Table 6. Predicted[/a] vs. Observed[/b] Margins of Safety (MOE) for Backpack Applicators of Glyphosate

MOE	Systemic (EIS[c])	Reproductive (EIS[c])
Predicted MOE @ 1 lb. a.i.		
Realistic	1068 (389)	344 (125)
Conservative	552 (201)	178 (65)
Worst Case	434 (87)	140 (28)
Observed MOE (n=20)		
10% dermal absorption	552	178
3.7% dermal absorption	1456	470

[a] NOEL/Forest Service EIS[1] MOE for each model, normalized to mean study application rate of 1 lb./acre
[b] NOEL/mean EAD; Backpack Applicator 0.055 mg/kg at 10% absorption or EAD of 0.021 mg/kg at 3.7% absorption.
[c] MOE from Table F-54 of EIS document using 2.75 lb.. a.i/ac for realistic and conservative. The 5 lb. a.i/ ac was used for the worst case scenario.

The observed effect in a multi-generational rat reproduction study used to obtain the 10 mg/kg/day NOEL in the EIS[1] was an "increase in focal tubular dilation of the kidney at 30/mg/kg/day", and is now considered "spurious rather than a glyphosate-related effect"[15]. This effect was not observed in a two-generation rat reproduction study at dose levels up to 1500 mg/kg/day, the highest dose tested[15]. Currently the US EPA uses a developmental toxicity study in rabbits with a NOEL of 175 mg/kg/day to calculate a reference dose (RfD) for dietary exposure[15]. This RfD is 2.0 mg/kg/day and incorporates an uncertainty factor of 100. "The RfD is determined by using the toxicological endpoint or the NOEL for the most sensitive mammalian toxicological study." [15] At the time of the EIS, animal studies were classified as having inadequate animal evidence of carcinogenic potential. With the completion of a repeat rat chronic feeding/carcinogenicity study, the reviewers classified glyphosate as showing "evidence of noncarcinogenicty in humans, based upon lack of convincing carcinogenicity evidence in adequate studies in two animal species."[15]

In 1996 a risk assessment of glyphosate was completed for the Forest Service by Syracuse Environmental Research Associates, Incorporated[25]. Exposures were calculated from the worker studies that included both dermal and urinary monitoring. Since no glyphosate was detected in the urine, they used minimum detectable levels (0.01 - 0.085 μg/mL) and assumed a urinary output of 2000 mL per day to calculate exposure. They normalized data to μg/kg body weight/lb. active ingredient (μg/kg bw/lb. a.i.) and used a plausible range of exposures from 0.25 to 9.0 μg/kg bw/lb. a.i.. This was consistent with their range of glyphosate absorption (0.8 - 2.4%). They determined that passive monitoring in the study by Lavy (1992) over estimated exposure by 40 times. Using the 3.7% dermal absorption from Thongsinthusak (1996) and dividing by the pounds a.i. applied from Table 3, our range of exposure would be 4.0 to 26.0 μg/kg bw/lb. a.i. Thus, exposures measured in this study are at the high end of their plausible exposure calculations when using the higher glyphosate absorption rate.

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Appendix 1 Deviations from protocol, SOP and GLP requirements.

Study Day	**Date**	**Protocol Requirement**	**Deviation**	**Effect on Study/Sample(s) Involved**
SE41 SE42	7/12/95 7/13/97	All applications will abide by California Code of Regulations and Forest Service Codes. [I. E. 1.]	Some workers wore contaminated gloves or did not wear gloves daily during all procedures. 3CCR Section 6738 requires new or cleaned gloves daily.	No effect on overall study results. Some worker hand exposure results could decrease. Forest Service codes are not unknown.
SE41	7/12/95	All wipe samples for each region are to be discreet for each worker for the entire workday. [I. E. 8. b) (4) (d)]	PM wipe samples for worker 4 and 6 were put in each others labeled jars. Samples match am wipes of jar labels but contain the others pm samples.	No effect on overall study results. Data would fall within 50 fold range of results. Discreet worker result could increase or decrease slightly.
SE41 SE42	7/12/95 7/13/97	Beginning and end time of loading for each worker will be recorded. [I. E. 7. e) (1)]	Did not record all load times for all workers each day.	No effect on study data. Load times were not used to calculate overall exposure. Data collected for information on workday.
SE41	7/12/95	Beginning and end time of applications for each worker will be recorded. [I. E. 7. g) (1)]	Did not record final application times of last load for workers eight and ten.	No effect on study data. Application times were not used to calculate overall exposure. Data collected for information on workday.
SE42	7/13/95	Inhalation monitoring will be conducted for the duration of each study day. [I. E. 8. a) (6)].	Cassette for worker 2 was lost one hour into study	No effect inhalation exposure Cassette was replaced and allowed to run for rest of workday. Inhalation did not significantly contribute to overall exposure
SE41 SE42	7/12/95 7/13/97	Inhalation monitoring will be conducted for the duration of each study day. [I. E. 8. a) (6)].	Air pumps were run an additional 10 to 15 minutes at end of study day to allow time to get dermal samples from workers.	No effect on study. Additional run time was subtracted from total minutes. Only time pump was worn by worker was used in the calculations.
SE41 SE42	7/12/95 7/13/97	In process audits will include study subject consent process. [I. E. 16. b)]	Consent process was inspected but no report was filed.	No effect on study data.

Appendix 1 Deviations from protocol, SOP and GLP requirements (continued).

Study Day	Date	SOP Number	SOP Requirement	Deviation	Effect on Study
SE41, SE42	07/12/95 07/13/95	WHS-AD01	Reviews shall be kept current with the stipulated time frames	The following WHS SOPs had lapsed review periods during this portion of the study: AD01 - AD05, EQ01, EQ17 - EQ19, FO07 - FO08, PS01, PS03, QA01 - QA03, SA01, TS02	Negative: While all pertinent SOPs were followed, the non-adherence to the required review schedule suggests that the controls for the administrative process of initiating and coordinating the necessary reviews are inadequate.
SE41, SE42	07/12/95 07/13/95	WHS-FS07	Data entries shall be dated on the day of entry. Each error shall be dated and initialed	Some forms had undated error corrections and some forms were not initialed and dated by the person recording the data	No effect on study data.

Study Day	Date	GLPS Section	GLP Requirement	Deviation	Effect on Study
SE41 SE42	7/12/95 7/13/95	160.405(a)	Each batch of the test substance shall be determined before its use.	The test substance characterization was not documented before its use in the study as required in 40 CFR 160.105(a).	None; the test substance was a registered product with known physical characterization. Samples of the lot number were analyzed and retained
SE41 SE42	7/12/95 7/13/95	160.63	All equipment used to collect raw data shall be adequately tested, calibrated and/or standardized; SOPs shall be in place.	Supplemental and support data such as weather data were not collected in compliance with GLP.	None; weather data were not used in data analyses and parameters were not critical to performance or integrity of the test substance. Data were collected to qualitatively assess the range of environmental conditions.
SE41 SE42	7/12/95 7/13/95	160.35(c), 160.63, 160.81(a)	All QA responsibilities procedures shall be in writing. All equipment shall have SOPs. The testing facility shall have all necessary SOPs.	All SOPs required by the regulations may not have been in place at the time of study conduct.	Possibly negative; without SOPs, some necessary procedures may have been neglected.

Appendix 2 Exposure monitoring samples
Raw data reported as µg glyphosate acid

Sample Date	Worker	hand wipes (hands)	face/neck wipes (face/neck region)	T-shirts (upper body)	socks (legs/feet)	Air filters (inhalation)
7/12/95	1	3826.2	854.6	32081.2	1657.8	7.64
	2	4593.0	1538.4	8196.2	20613.4	7.76
	3	24385.4	3752	11040.6	21603.6	6
	4	6315.8	1327.8	20887.2	383.6	3.91
	5	7942.4	1594.2	4796.8	607.0	6.15
	6	15180.2	1570.4	11705.8	1807.8	3.55
	7	58427.0	3527.4	13953.0	2181.8	6.91
	8	11225.4	2256.4	6077.2	1051.0	4.34
	9	4005.0	967.0	11672.8	7357.2	5.41
	10	6249.0	1295.6	13048.4	18941.8	6.52
7/13/95	1	1623.6	301.4	18990	910.4	8.4
	2	3100	866.2	8115.8	3883.4	5.21
	3	5671.6	1106.4	25324.4	19305.2	6.81
	4	2017.8	638.6	7868.4	472.6	8.41
	5	4243.8	1286.6	9388.2	821.6	3.62
	6	2870.4	592.6	7314.4	700.2	4.3
	7	6449.6	1245.8	10100.8	2472.8	6.17
	8	1416.6	572	8762.2	484.6	5.85
	9	2651.2	752.4	4416.6	3108.8	12.58
	10	3133.8	550.2	8472.2	981.8	6.59

Appendix 3 Test Substance and Tank Mix samples
Raw data reported as glyphosate acid

Sample	Sample description	% recovery	µg/g
SE41-1077	Test substance (Accord®)	98	0.12
SE41-1066	Tank mix 1	108	0.13
SE41-1067	Tank mix 1	111	0.14
SE41-1069	Tank mix 2	99	0.12
SE41-1070	Tank mix 2	95	0.12
SE41-1072	Tank mix 3	105	0.13
SE41-1073	Tank mix 3	111	0.14
SE42-1066	Tank mix 1	108	0.13
SE42-1067	Tank mix 1	100	0.13
SE42-1069	Tank mix 2	108	0.14
SE42-1070	Tank mix 2	98.8	0.12
SE42-1072	Tank mix 3	106	0.13
SE42-1073	Tank mix 3	97	0.12

Appendix 4 Field fortification samples
Raw data reported as glyphosate acid

Sample	Sample	μg/sample	Field fortification levels
Air filter AE	SE41-1040	5.08	5.0 μg for air filters
Air filter AE	SE41-1041	5.50	
Air filter AE	SE41-1042	5.78	
Air filter AE	SE42-1040	5.77	
Air filter AE	SE42-1041	5.28	
Air filter AE	SE42-1042	4.64	
Socks	SE41-1043	320.2	250.0 μg/sample for dermal matrices
Socks	SE41-1044	252.0	
Socks	SE41-1045	243.0	
Socks	SE42-1043	246.2	
Socks	SE42-1044	249.2	
Socks	SE42-1045	249.6	
T-Shirts	SE41-1046	226.0	
T-Shirts	SE41-1047	231.6	
T-Shirts	SE41-1048	209.0	
T-Shirts	SE42-1046	244.4	
T-Shirts	SE42-1047	250.2	
T-Shirts	SE42-1048	245.8	
wipes	SE41-1049	250.0	
wipes	SE41-1050	238.8	
wipes	SE41-1051	262.4	
wipes	SE42-1049	241.2	
wipes	SE42-1050	246.6	
wipes	SE42-1051	248.6	

Appendix 5: Personnel air sampling

Sample Number	Worker	Pump flow[a] 1 average (Pump flow L/min.)	minutes[b] pump 1	Pump flow 2 average (L/min pump 2, if needed)	minutes pump 2	Liters collected[c]	PIE mg[d]
SE41-1014	101	2.10	525			1103	0.131
SE42-1014	101	2.00	413			826	0.151
SE41-1015	102	2.10	526			1105	0.133
SE42-1015	102	1.95	339			661	0.113
SE41-1016	103	2.10	521			1094	0.103
SE42-1016	103	2.05	420			861	0.120
SE41-1017	104	1.70	522			887	0.083
SE42-1017	104	1.95	421			821	0.155
SE41-1018	105	2.05	519			1064	0.108
SE42-1018	105	1.75	410			718	0.074
SE41-1019	106	1.00	245	2.20	279	859	0.078
SE42-1019	106	1.95	158	1.80	261	778	0.083
SE41-1020	107	2.05	520			1066	0.121
SE42-1020	107	1.95	415			809	0.114
SE41-1021	108	2.05	520			1066	0.076
SE42-1021	108	1.95	416			811	0.108
SE41-1022	109	2.00	521			1042	0.097
SE42-1022	109	1.65	409			675	0.274
SE41-1023	110	2.10	519			1090	0.112
SE42-1023	110	1.80	411	0		740	0.132

[a] Pump flow = (Start flow + End flow)/2

[b] minutes = (time off - time on)

[c] Liters collected = flow average x minutes

[d] PIE mg glyphosate salt =

$$\frac{\text{(glyphosate acid µg x 1.348 correction factor for glyphosate salt) x 26.7 breathing rate}^{12}\text{ x minutes}}{\text{Liters collected}}$$