ESTIMATION OF EXPOSURE OF PERSONS IN CALIFORNIA TO THE PESTICIDE PRODUCTS THAT CONTAIN

DIQUAT DIBROMIDE

BY

Tareq A. Formoli, Associate Environmental Research Scientist
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California Environmental Protection Agency
Department of Pesticide Regulation
Worker Health and Safety Branch
1020 N Street, Room # 200
Sacramento, California 95814

ABSTRACT

Diquat dibromide is a non-selective, contact herbicide that is used in California for desiccation of seed crops. It is also used for rights-of-way weed control, landscape maintenance, and aquatic weed control. A total of 64 illnesses and injuries associated with the use of diquat dibromide were reported in California from 1984 through 1992. Most of these incidents occurred due to lack of required protective clothing and/or inadequate training. Approximately 60 percent of all illnesses and injuries involved applicators using hand-held equipment. Prolonged dermal exposure to diquat dibromide can cause severe skin damage. Systemically absorbed diquat dibromide does not selectively accumulate in lung tissues. Diquat dibromide is excreted rapidly from the human body, primarily in urine, following an intravenous injection. Its dermal absorption rate is estimated at 1.4 percent in 24 hours in humans. Diquat dibromide exposure monitoring studies and surrogate data were used to estimate workers' absorbed daily dosages.

This report was prepared to be included as Volume 2 in the risk characterization document for diquat dibromide. The risk assessment is being conducted because of chronic, and developmental toxicities observed in toxicity testing in laboratory rats and rabbits.

Department of Pesticide Regulation
Worker Health and Safety Branch

Human Exposure Assessment

Diquat Dibromide

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CHEMICAL/PHYSICAL PROPERTIES

Diquat dibromide is the common name of 6,7-dihydrodipyrido (1,2-a: 2',1'-c) pyrazinediium dibromide. Its chemical formula is $C_{12}H_{12}Br_{2}2N_{2}$ with a molecular weight of 344.1 daltons. It is completely soluble in water, but insoluble in non-polar organic solvents. The solids melt at 300 ^{o}C. The technical material is available only as a liquid. Diquat dibromide is stable in neutral or acidic solutions, but unstable in alkaline solutions and is corrosive to metals. Diquat dibromide is a non-flammable, non-volatile product. Traces of ethylene dibromide are present in the technical material as manufacturing impurities. The word "diquat" used hereafter refers to diquat dibromide.

U.S. EPA STATUS

In June 1986, the United States Environmental Protection Agency (U.S. EPA) issued a reregistration standard based on its assessment of the available data on diquat. The standard identified numerous data gaps, and therefore made conclusions that were subject to change. It concluded that (a) until additional required chronic toxicity data were made available and evaluated, diquat was not considered to cause oncogenic, teratogenic or reproductive effects; (b) the presence of ethylene dibromide as an impurity would not pose a significant risk to human health with the current uses of diquat; and (c) diquat appeared to be acutely toxic through dermal exposure. Consequently the U.S. EPA identified the missing data to be developed and determined certain label restrictions and revisions including a restricted use classification, signal word revision, dermal exposure precaution, crop rotation restriction, reentry interval and protective clothing requirements. As certain data were developed and reviewed, the U.S. EPA changed its position on some label restrictions, including restricted use classification, signal word change, and protective clothing requirements.

USAGE

Diquat is a non-selective, contact herbicide that is used for desiccation of certain seed crops and potatoes. It is also used for non-crop and aquatic weed control. As of June 26, 1995, there were 38 products registered in California that contain diquat. The majority of these products are labeled for non-crop uses, mainly for industrial, home garden, rights-of-way, landscape maintenance and aquatic weed control. The agricultural products are for use as desiccants on seed crops (alfalfa, clover, grain, and soybeans) and potatoes. Based on the pesticide use reports for 1992, a total of 89,000 lb. of diquat were used in California mostly on alfalfa (30% of the total use), rights-of-way (36%) and landscape maintenance (18%) (DPR, 1994). Aquatic use accounted for less than two percent of the total use. Diquat can be used by aerial or ground equipment for agricultural uses. Diquat applications to alfalfa are mainly by air. Diquat right-of-way applications are mostly made by the California Department of Transportation, and county and city employees using vehicle-mounted application equipment. Aquatic application is done by ground equipment.

FORMULATION

All diquat products in California are liquid. The products for agricultural uses are 35.3% diquat formulations containing 2.0 lb. active ingredient (a.i.)/gal. The products for manufacturing uses are also 35.3% formulations. Other formulations are mostly 0.3% to 5.0% diquat. The rate of application is 0.25 to 0.5 lb. a.i. (cation) per acre for agricultural uses, 2.0 to 4.0 lb. a.i. (cation) per surface acre for aquatic uses and 0.5 to 1.0 lb. a.i. (cation) in 100 gal. of water for non-crop terrestrial uses.

LABEL PRECAUTIONS

Products with 35.3% diquat have the toxicity category II signal word of "warning" for their acute oral, dermal and inhalation toxicities. Formulations with lower than 35.3% diquat are either toxicity category II or III. Hazards of ingestion, inhalation and dermal contact have been indicated on these product labels. A statement of practical treatment is given for accidental exposures. The product labels require workers handling diquat to wear the following personal protective equipment (PPE):

- Coveralls over short-sleeved shirt and short pants.
- Waterproof gloves.
- Chemical resistant footwear and socks.
- Protective eyewear.
- Chemical resistant headgear for overhead exposure.
- Chemical resistant apron when cleaning equipment, mixing, or loading.

According to the federal worker protection standards (WPS) for agricultural pesticides [40 CFR 170.240(d)(4-6)], when using closed systems mixing/loading, enclosed cabs, or enclosed cockpits, the PPE requirements for mixer/loaders may be reduced to work clothing (long-sleeved shirt and long pants) plus chemical resistant apron and gloves and for applicators may be reduced to work clothing. The reentry interval to treated terrestrial areas is 24 hours. Entry into treated aquatic areas is prohibited while treatment is in progress. The reentry to treated water for swimming is 24 hours. The use of treated water for domestic purposes, animal consumption, and crop irrigation is prohibited for 14 days after application. Some product labels for home garden uses warn users to keep children and pets out of the treated area until spray mist has completely dried.

WORKER ILLNESSES

A total of 64 illnesses and injuries associated with the use of diquat alone or in combination with other pesticides have been reported in California from 1984 through 1992 (PISP, 1994). The incidents included eye injuries (24 cases), skin injuries (17 cases), eye/skin injuries (two cases), systemic illnesses (20 cases), and respiratory illness (one case). There was one suicidal death from ingestion of diquat in 1989. Illnesses and injuries due to diquat alone accounted for 40 incidents (including three non-occupational), and four required hospitalization ranging from three to 19 days. The longest disability incurred was 74 days which resulted from a prolonged and extensive skin exposure, requiring skin grafting. Most of the worker illnesses and injuries were due to lack of required protective clothing and equipment, or/and inadequate training. Symptoms such as nausea, dyspnea, and dizziness have been reported. Skin or/and eye injuries such as rashes, burns, conjunctivitis as well as loss of toe nails were observed. The majority of incidents occurred to the pesticide applicators. Applicators using hand-held equipment accounted for 60 percent of all illness and injury cases. Other incidents occurred during mixing/loading, foliar contact and incidental activities during handling.

DERMAL TOXICITY

Data collected in 1966 on the handling of diquat indicate incidents of human skin discoloration and nose bleeding (Summary Report, 1966). These data were presented without further details. Severe skin burns as a result of prolonged and extensive exposure to diquat have also been reported (Manoguerra, 1990). Systemically absorbed diquat does not selectively accumulate in lung tissue and pulmonary injury by diquat is less prominent than by paraquat. Diquat has severe toxic effects on the central nervous system (Morgan, 1989). Damage and discoloration of fingernails caused by frequent exposure to concentrated solutions of diquat were also reported. Rashes, blisters and transient skin discoloration were reported as a result of exposure to the concentrated commercial preparation. Accidental ingestion of a small amount of diquat by a person caused diarrhea and oral ulceration (FAO, 1971). Breathing spray mist can cause nasal, throat and respiratory tract irritation (MIB, 1981). Diquat did not cause skin sensitization in guinea pigs tested with formulated products (Thompson, 1985 and Robbins, 1987).

DISLODGEABLE FOLIAR RESIDUE

Most of the work activities following diquat applications to crop and non-crop terrestrial areas are mechanical. Dermal exposure to foliar residues is considered insignificant compared to dermal exposure during handling.

METABOLISM

Male albino Wistar rats were administered ^{14}C-diquat by stomach tube (1.8 uCi, 45 mg/kg) or by subcutaneous injection (5.6 uCi, 10 mg/kg) and kept in metabolism cages for four days (Mills, 1976). Urine and feces were collected daily and analyzed collectively from groups of five rats using a liquid scintillation spectrometer. Rats that were given a single oral dose excreted 6.3% and 89.3% of the administered radioactivity in the urine and feces, respectively, within four days, mainly as diquat. Urine contained 5.1% diquat, and 0.2% diquat monopyridone and 0.1% diquat dipyridone (diquat metabolites). Feces contained 57% diquat and 4.1% monopyridone. Rats that received a subcutaneous injection excreted 87.1% and 4.8% of the administered radioactivity in urine and feces, respectively, within four days, mainly as diquat.

Tissue distribution of diquat was studied in male and female albino Wistar rats (Litchfield, 1973). Rats were fed diquat (250 ppm diquat cation) in their diet. A group of 10 rats were sacrificed at two, four, and eight weeks. The brain, lungs, liver, kidneys, hind leg muscles, stomach, small and large intestines were analyzed for diquat using colorimetric determination. Recovery of diquat injected into the tissue was 90 - 95%. Diquat presence in tissues was measurable in two weeks. No sex differences were observed. Diquat tissue concentration was generally lower than that of paraquat, particularly in lungs. No diquat was detected in tissues (MDL of 0.05 ug/g) within one week of return to a normal diet.

Male mice were subcutaneously injected with 0.2 mL ^{14}C-diquat, 50 mg cation/kg. Two mice were killed by exposure to diethyl-ether at 10 minutes, one hour, 24 hours, and 72 hours after the injection (Litchfield, 1973). Whole body autoradiography showed that radioactivity was distributed throughout most tissues at 10 minutes. Radioactivity level declined in most tissues but intestinal epithelium and urine radioactivity increased at one hour. At 24 hours, radioactivity was observed only in the small and large intestines and bladder. At 72 hours, radioactivity was observed only in stomach and intestinal contents.

A British Saana goat was administered a single oral dose of 145 mg/kg diquat ion (Griggs, 1970). Milk and excreta were collected daily. Samples were analyzed by scintillation counting using a Packard Tricarb spectrometer. Approximately 96% of the radioactive dose was recovered in feces (94%), urine (2%), and milk (traces) within seven days, mainly as diquat.

A single oral dose (20 or 5 mg/kg) of ^{14}C-diquat was given to a cow (Stevens, 1966). Only traces (0.001 to 0.015%) of the administered dose was found in milk and 2.6% in urine in seven days. Tissues and organs of a 120-Kg calf slaughtered 24 hours after dosing with 1.38 g of ethylene bridged-labeled ^{14}C-diquat were analyzed. The kidney and liver contained 0.66 ppm and 0.21 ppm diquat residues, respectively. Other tissues and organs contained <0.05 ppm diquat residues.

In order to determine the extent of human elimination of diquat in urine, a dose of one uCi ^{14}C-diquat was administered intravenously (iv) to six male human volunteers (Feldmann, 1974). Urine samples were collected for five days at four-hour intervals followed by a 12-hour interval in the first day and every 24 hours for the remaining four days. Samples were analyzed by wet ashing 5 mL of the urine and trapping all of the carbon as carbon dioxide (CO_2) in ethanolamine. The trapped CO_2 was diluted and counted with a scintillation counter. Total urinary elimination was measured at 61.2 $\pm$ 16.0% of the administered dose in five days. Approximately 90% of the excreted dose was eliminated in the first 24 hours following administration.

DERMAL ABSORPTION

In Vitro:

Dermal absorption of diquat has been studied in vitro in humans and animals, using glass diffusion cells (Corrigan, 1989(a)). Human abdominal or rat dorsal whole skin was taken post mortem and mounted in the diffusion cell between the donor and receptor chambers. Different dilutions of diquat (1 mg/mL, 5 mg/mL, and 50 mg/mL) were applied to the skin at the rate of 0.1 mL/cm^2. ^{14}C-diquat was diluted in these solutions to a final activity of about 4 uCi/mL. A Betamatic II liquid scintillation spectrometer was used for analysis. A measured volume of 0.9% saline was placed into the receptor chamber. Samples of 50 uL were taken from the receptor chamber at different time intervals. A lag time of about two hours for rat skin and 15 hours for human skin was observed until initial absorption. The initial period of increasing absorption was followed by a steady state. A steady state absorption rate was calculated for each dilution as shown in Table 1.

Table 1. In Vitro Dermal Absorption of Diquat in Human and in Rat

# of reps.	Dilution mg/mL	Application Rate (mg/cm^2)	Dermal Absorption Rate ug/cm^2/hr	ug/cm^2/24 hrs	%/24 hrs
Human:					
7	1	0.1	0.06	1.44	1.44
8	5	0.5	0.18	4.32	0.86
7	50	5.0	0.98	23.54	0.47
Rat:					
6	1	0.1	0.23	5.54	5.52
5	5	0.5	1.01	24.24	4.85
5	50	5.0	9.55	229.20	4.58

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Similar in vitro dermal absorption studies with human skin, using different dilutions of diquat, have resulted in dermal absorption rates that ranged from 0.18 to 1.4% (Corrigan, 1989(b), Scott, 1985).

In Vivo:
Dermal absorption of diquat was studied in rats (Brorby, 1988). ^{14}C- labeled diquat was dissolved in water and applied (0.05 mg, 0.5 mg, and 5.0 mg) to the shaved dorsal trunk of rats. Urine, feces, and volatiles were collected following the dermal treatment. Approximately 2.5%, 3.6%, and 3.4% of the applied dose were systemically absorbed in 24 hours in rats treated with 0.05 mg, 0.5 mg, and 5.0 mg of ^{14}C-labeled diquat, respectively.

Human dermal absorption of diquat was also studied in vivo (Feldmann, 1974). ^{14}C-diquat was applied to the ventral forearm of six normal male human volunteers at four ug/cm^2. This is equivalent to a thin film of 0.25% diquat solution. The dose was dissolved in a small amount of acetone and applied to the skin. The acetone was evaporated by gentle blowing during application. The application sites remained unoccluded. The volunteers were advised not to wash their forearms for 24 hours. Urine samples were collected for five days at three four-hour intervals followed by a 12-hour interval during the first day and every 24 hours for the remaining four days. Samples were analyzed by wet ashing 5 mL of the urine and trapping all of the carbon as carbon dioxide (CO_2) in ethanolamine. The trapped CO_2 was diluted and counted with a scintillation counter. The results were corrected for incomplete urinary excretion of diquat. Only 0.3 $\pm$ 0.1% of the administered dose was recovered in five days.

In evaluating the parameters affecting dermal absorption, it was noted that occluding the application site increased diquat dermal absorption by 3.5 fold to 1.4% (Wester, 1985). Damaged skin absorbed 9.5 fold more diquat (3.8%) than non-occluded normal skin of human volunteers. A dermal absorption of 1.4% will be used in calculating diquat absorbed daily dosages for regulatory purposes.

WORKER EXPOSURE

Aquatic Use
Workers were monitored during normal applications of diquat for aquatic weed control (Wojeck, 1983). Each worker wore a long- or short-sleeved shirt, long trousers, socks and heavy shoes or boots. Two application methods were used. For control of water hyacinths and other floating vegetation, diquat was applied from an airboat by two workers, an applicator using hand-operated spray equipment and a driver. Diquat was used at a rate of 1 qt. (0.5 lb. a.i./acre) formulated product per acre (final spray mixture of 1.76% diquat). Another aquatic herbicide, Komeen® (2 qt./acre) was also used as a tank mix with diquat.

For control of hydrilla, diquat was injected into the water at a rate of 2 gal. (4 lb. a.i./acre) formulated product per acre (final spray mixture of 4.41% diquat), using an invert system. The crew for this method consisted of a gloved mixer who prepared the tank mix on the shore and an applicator who drove the airboat and injected the diquat into the water. The applicator also assisted in pumping the spray mixture to the tank on the boat.

Workers applied diquat two to five hours/day, four days a week. There were three handgun spray crews and one invert system crew. The workers were monitored three times over a three-month period. Potential dermal exposure of workers was monitored by placing dermal alpha-cellulose pads at 10 locations on the body outside of the clothing. Hand exposure was estimated from two consecutive hand rinses with 100 mL water or from patches that were cut from palms and backs of cotton sampling gloves worn by each worker. Anderson air samplers with polyurethane foam plugs were used to collect air samples near the breathing zone of workers. Urine samples were also collected, once prior to the monitoring and then each day during the monitoring study.

Diquat recoveries from cotton gloves and alpha-cellulose pads were 94% and 93%, respectively. The recovery from foam plugs was 80%. Samples were analyzed using a Beckman DK-2A spectrophotometer. Urine samples were analyzed separately. Diquat in urine ranged from 0.007 to 0.047 ppm. Respiratory exposure was reported <0.1% of the total body exposure. Workers' potential dermal exposure was estimated from residues found on the alpha-cellulose pads and cotton gloves or hand rinses. Potential dermal exposure in Table 2 was calculated according to the body surface areas and body weight described in the Exposure Assessment

Guidance (Thongsinthusak et al., 1993). Gloves as a medium to assess hand exposure typically overestimate that exposure by up to nine fold when compared with hand washes (Smith, 1991).

Table 2. Estimate of Mixer/Loaders and Applicators' Exposure to Diquat During Application of Aquatic Weeds

	Handgun Application (0.5 lb. a.i./acre)		Invert Application (4.0 lb. a.i./acre)	
	Applicator	Boat Driver	Applicator	Mixer
n	9	9	3	3
	ug/8-hour day	ug/8-hour day	ug/8-hour day	ug/8-hour day
Head	235.20	50.40	184.80	50.40
B. Neck	17.12	4.28	4.28	4.28
F. Neck	46.72	5.84	35.04	5.84
Back	552.64	138.16	138.16	138.16
Chest	1105.28	138.16	828.96	138.16
Upper arms	118.32	59.16	236.64	59.16
Forearm	387.52	96.88	290.64	290.64
Thigh	7032.96	146.52	146.52	586.08
lower leg	1178.40	196.40	98.20	1178.40
Feet	602.88	100.48	50.24	602.88
Hand	3513.60	1098.00	658.80	805.20
Potential Dermal	14790.64	2034.28	2672.28	3859.20
Daily Dermal[a]	6862.36	1600.48	1457.03	3029.80
Daily Dermal[b]	686.24	160.05	145.70	302.98
	(ug/kg/day)	(ug/kg/day)	(ug/kg/day)	(ug/kg/day)
ADD[c]	0.13	0.03	0.03	0.06
ADD[d]	0.51	0.12	0.03	0.06

a - Short-sleeved shirt and short pants, providing 90% protection to covered areas.

b - Coveralls (over short-sleeved shirt and short pants), waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear, providing 90% protection.

c - Based on an 8-hour workday, male body weight of 75.9 kg (Thongsinthusak, et al., 1993), and dermal absorption of 1.4% (see dermal absorption section). Samples with non-detected levels were assumed to contain residues at half of MDL, MDL = 0.01 ug/cm^2.

d - Corrected for the highest label rate (2 lb. a.i./acre) for floating weeds.

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Terrestrial Crop and Non-Crop Uses

Diquat worker exposure data are very limited. In the absence of worker exposure data for diquat, paraquat worker exposure data would be a suitable surrogate. Paraquat is also a bipyridylium herbicide that has chemical and physical properties and use patterns similar to that of diquat. The application equipment is also similar for these two products, except a closed mixing and loading system is required when handling paraquat. A closed mixing and loading system is not a requirement for handling diquat.

Only one worker exposure study of terrestrial use of diquat was available. This study was published in the open literature in German (Sawinsky, 1977). A summary is available in English. The study monitored workers' exposure during aerial application of diquat. It did not describe the rate of application or the type of protective clothing and equipment worn by the workers. The duration of application was approximately four hours. Air samples taken from the cockpit contained a mean value of 4.5 ug/m^2 diquat and residue samples taken from pilots' clothing contained a mean value of 61.5 ug/100 cm^2 diquat during the four hours of monitoring. No residues were detected in the cockpit air when the air filter and ventilation were in operation. Clothing samples of the mixer and the loader contained 3500 ug/100 cm^2 and 8700 ug/100 cm^2 diquat, respectively, during the monitoring period. Urine samples were taken only from the ground crew. Urinary diquat residues ranged from non-detectable levels to 30 ug/100 mL sample. The mixer's and the loader's mean urinary diquat were 6.3 ug/100 mL and 19.6 ug/100 mL, respectively. Workers' dermal exposure can not be estimated from residues on clothing samples since it was not clear whether sufficient number of samples were taken from various parts of the clothing. The mixer and the loader exposures were estimated from residues found in their urine corrected for incomplete diquat urinary excretion (Feldmann, 1974), 1400 mL daily urinary output (Guyton, 1969), and 75.9 kg body weight. The mixer and the loader Absorbed Daily Dosages (ADD) were 3.8 ug/kg/day and 11.8 ug/kg/day, respectively. Mixing and loading is normally performed by one worker. The estimate of ADD for diquat aerial mixer/loader spending as much time mixing as loading is 7.8 ug/kg/day. The exposure to a mixer/loader during ground application can be conservatively estimated from the exposure data for mixer/loaders of diquat during aerial application.

Table 3. Diquat Aerial Application Flaggers' Estimated Exposure Using Paraquat Data as Surrogate

	Flagger 1 Trial I	Flagger 2 Trial I	Flagger 1 Trial II	Flagger 2 Trial II
	ug/per/day	ug/per/day	ug/per/day	ug/per/day
Head	6384.72	341.64	8074.57	286.54
B. Neck	207.36	29.38	67.39	114.05
F. Neck	732.10	7.08	2432.45	113.36
Back	2994.28	1441.69	1996.19	3659.67
Chest	17189.38	166.35	57113.09	2661.58
Upper arm	3239.04	323.90	5552.64	2059.10
Forearm	2647.68	264.77	4538.88	1683.17
thigh	9696.96	581.82	69818.11	2973.73
lower leg	4235.48	129.66	25499.33	2074.52
feet	2214.64	67.80	13333.06	1084.72
Hand	2064.00	163.20	2544.00	93.60
Potential Dermal	51605.63	3517.29	190970.00	16804.05
Daily Dermal[a]	21797.94	1254.90	69937.68	6585.37
Daily Dermal[b]	2179.79	125.49	6993.77	658.54
Daily Resp.	101.12	0.19	0.19	9.47
ADD[c]	2.14	0.03	1.60	0.30
ADD[d]	5.95	0.09	4.43	0.84

a - Short-sleeved shirt and short pants, providing 90% protection to covered areas.
b - Coveralls (over short-sleeved shirt and short pants), waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear, providing 90% protection.
c - Based on an 8-hour workday, female body weight of 61.5 kg (Thongsinthusak, et al., 1993), dermal absorption of 1.4% (see dermal absorption section), and respiratory uptake and absorption of 100%. Samples with non-detected levels were assumed to contain residues at half of MDL, MDL = 0.01 ug/cm^2.
d - Corrected for the highest label rate (0.5 lb. a.i./acre).

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A worker exposure study of paraquat during an aerial application to cotton was conducted in the San Joaquin Valley in 1979 to estimate the exposure of pilots, mixer/loaders, and flaggers (Chester and Ward, 1981). This study was used as a surrogate to estimate the exposure of pilots and flaggers to diquat during aerial application. Mixer/loaders' exposure can not be estimated from this study since a closed mixing/loading system was used.

Table 4. Diquat Aerial Application Pilots' Estimated Exposure Using Paraquat Data as Surrogate

	Pilot 1 Trial I	Pilot 2 Trial I	Pilot 1 Trial II	Pilot 2 Trial II
	ug/per/day	ug/per/day	ug/per/day	ug/per/day
Head	12.10	12.10	12.10	11.02
B. Neck	1.03	1.03	1.03	0.86
F. Neck	1.40	1.40	1.40	1.18
Back	33.16	33.16	33.16	27.72
Chest	33.16	33.16	33.16	27.72
Upper arm	14.20	14.20	14.20	11.57
Forearm	11.63	11.63	11.63	9.46
thigh	35.16	35.16	35.16	32.32
lower leg	23.57	381.80	23.57	21.61
feet	12.06	195.33	12.06	11.30
Hand	460.80	249.60	1008.00	139.20
Potential Dermal	638.26	968.57	1185.46	293.97
Daily Dermal[a]	491.62	334.57	1038.82	166.44
Daily Resp.	0.34	0.34	0.34	2.02
ADD[b]	0.09	0.06	0.19	0.04
ADD[c]	0.26	0.18	0.54	0.12

a - Long-sleeved shirt, long pants, and footwear providing 90% protection to covered areas and using closed cockpit plane.

b - Based on an 8-hour workday, male body weight of 75.9 kg (Thongsinthusak, et al., 1993), dermal absorption of 1.4%% (see dermal absorption section), and respiratory uptake and absorption of 100%. Samples with non-detected levels were assumed to contain residues at half of MDL, MDL = 0.01 ug/cm^2.

c - Corrected for the highest label rate (0.5 lb. a.i./acre).

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One pint of Ortho Paraquat CL containing 1.4 lb. a.i./gallon was used in 10 gallons of water with one pint of X-77 (as an adjuvant) and three to four lb. of Tumble Leaf® (sodium chlorate) as a defoliant per acre on the first trial. Only Ortho Paraquat CL and X-77 were used in the second trial. A total of 1200 acres of cotton were sprayed using a Thrush Commander aircraft. Mixing and loading were done using a closed system. The pilots' clothing consisted of open necked short-sleeved shirt, T-shirt, long trousers, boots and hat. Flaggers wore protective cotton coveralls over normal clothing. Dermal exposure pads consisting of polythene-backed 100 cm^2 Whatman 542 filter papers were attached to the skin or clothing with adhesive tape at various locations. Hand exposure of the pilots and the flaggers was evaluated using bleached cotton gloves. Penetration through normal work clothing and protective clothing was evaluated by using white cotton T-shirts and by placing cotton Tubigrips (elasticized tubular support bandages) on the left leg (ankle to top of thigh) of each individual. Penetration through normal clothing was 5 percent based on chest and back pad ratio to the T-shirt for flaggers and the mixer/loader. Air samples from the breathing zones of workers were collected using personal air samplers to determine respiratory exposure. Body parts surface area and total dermal exposure were calculated according to methods described in the Exposure Assessment Guidance (Thongsinthusak, et al., 1993). Respiratory exposure was calculated using the instrument sampling rates and duration of exposure. The instrument sampling rate (three liters/minute) was corrected for human breathing rate during light work of 8 L/minute for females and 14 L/minute for males (Thongsinthusak, et al., 1993). Dermal and inhalation exposure of these workers to paraquat was used in Tables 3, and 4 to estimate dermal and inhalation exposure of flaggers and pilots to diquat.

Ground Applicator Exposure

In the initial exposure assessment document for diquat, the exposure to ground applicators was estimated using a study conducted in Florida where applicators were monitored for dermal and respiratory exposure to paraquat during post-harvest treatment of tomatoes (Wojeck, 1983). Dermal exposure was monitored by attaching alpha-cellulose pads to various parts of the body outside of workers' clothing. Hand exposure was estimated from two consecutive hand washes in water, or from areas cut from the palm and back of a pair of cotton sampling gloves. Respiratory exposure was measured by using Willson "Dustite" respirators fitted with 16-ply gauze backed with filter pads. The estimate of exposure, based on this study, ranged from 5.3 to 106 ug/kg/day for an applicator wearing long sleeved shirt, long pants, and shoes.

In a recent study, a more refined estimate of exposure to handlers of paraquat was made, using the biological monitoring technique (Meier, 1995). The study was conducted in Georgia and Alabama to investigate absorption of paraquat by 17 workers mixing/loading and applying Gramoxone Extra. This study meets the requirements of the EPA’s Good Laboratory Practices with a few exceptions, such as using commercially available product and not retaining the test substance containers, that would have no effects on study integrity. A single application of Gramoxone Extra (2.5 lb a.i./gal.) was made to pecan orchards at 0.94 lb a.i./acre. The mixing/loading operation was performed using open pour methods. The application was performed using ground boom spray equipment that was mounted on an open cab tractor. The spray booms of the tractors for two workers were in front of the driver’s seat. The amount of product handled during mixing/loading ranged from approximately 7 to 70 lb a.i., averaging 27 lb a.i. per day. All but one worker used a non-ionic surfactant. The duration of exposure ranged from 4 to 11 hours. Mixing/loading lasted 14 to 104 minutes. Wind was generally calm during handling, mostly below 7 MPH.

A complete 24-hour urine sample was collect from each worker one day prior, on the application (exposure) day, and for five days following the exposure day. Collected samples were kept frozen in the field laboratory and during delivery to the analytical laboratory. Field recovery samples were collected each day of monitoring by fortifying the urine samples from non-exposed individuals. Urine samples were analyzed for paraquat and creatinine. The detection limit was 5 ng/mL and the limit of quantitation was 10 ng/mL. The mean recovery for fortifications at 10, 20, and 50.1 ng/mL ranged from 100 to 108 percent.

Paraquat was detected in the urine of only six workers for the exposure day. No paraquat was detected in any samples collected during the two days following the exposure day, therefore, the samples collected on days 3, 4, and 5 after the exposure day were not analyzed. Results were corrected for 59 percent dose recovery in urine (Maibach, 1982). Based on the urine samples with detectable concentrations of paraquat for six workers, the ADD ranged from 0.07 to 0.44 ug/kg/day with an average of 0.21 $\pm$ 0.15 ug/kg/day. There is no clear correlation between paraquat absorption and the amount of product handled or the duration of exposure. These six workers handled an average of 34 lb. a.i. during an average 6.4 hours. They wore long- or short-sleeved shirts, long pants, hats, and boots. Only two of them wore eye glasses. No additional PPE was worn during mixing/loading by these six workers. Most (8 out of 11) of the workers with no detectable paraquat in their urine wore additional PPE such as gloves and apron during mixing/loading. The workers with no detectable paraquat in their urine samples were not included in the estimate of ADD so that dose was calculated based on actual measurements rather than lack of detection.

The diquat maximum application rate (0.5 lb. a.i./acre for agricultural uses) is approximately one-half the rate used in this study and diquat dermal absorption rate is approximately three fold greater than that of paraquat. To estimate the ADD for a mixer/loader/applicator of diquat, the average ADD of 0.21ug/kg/day calculated for workers in this study was adjusted for the differences in the application and dermal absorption rates. Using the above study as surrogate, the estimate of ADD for a diquat mixer/loader/applicator wearing a long- sleeved shirt, long pants, a hat, and boots and using a tractor equipped with a ground boom is 0.32 ug/kg/workday. Additional PPE, as required by the current product label, would further reduce the estimated ADD as evidenced by the non-detects routinely found with those workers using more PPE.

Home Garden and Landscape Use

No human exposure data are available for home garden or landscape uses of diquat. A human exposure study of paraquat during garden and yard application was used as surrogate to estimate the exposure of garden and landscape workers applying diquat (Staiff, 1975). A 0.44% paraquat pressurized product was applied by volunteers as spot treatment to control weeds in gardens and yards. Applicators' potential dermal exposure was monitored by attaching alpha-cellulose pads to various parts of the body or clothing. Hand exposure was measured by rinsing their hands in water. Respiratory exposure was measured by using filter pads (not specified) in the respirators worn by workers. A total of 15 exposure situations were studied. The volunteers wore no gloves or hats. Almost all exposure was on the hands. Only traces (<1.0 ug/cm^2) of paraquat were found on the lower legs. Respiratory exposure values were below the detection limit except for one sample containing 0.8 ug paraquat. Dermal exposure was calculated based on residues on the hands. Dermal exposure ranged from 0.01 mg/hr to 0.57 mg/hr with a mean of 0.29 mg/hr. Diquat garden and landscape workers' absorbed daily dosage (ADD) was estimated to range from 0.01 to 0.7 ug/kg/7-hour workday, with a mean of 0.4 ug/kg/7-hour workday, assuming 1.4% dermal absorption, body weight of 75.9 kg, and negligible inhalation exposure.

The exposure of applicators using hand-held equipment such as knapsack sprayers was estimated based on the exposure values of workers who applied 2, 4-D (Abbott, 1987). Workers (n=2) loaded premixed 2, 4-D into knapsack tanks and then applied the herbicide using the knapsack sprayers. Dermal exposure was measured by obtaining clothing samples from representative body parts. Gloves were used to measure hand exposure. The mean dermal exposure during loading from a total of eight replicates was 3.6 mg/lb. a.i., assuming the workers wore short-sleeved shirts, short pants, coveralls, waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear. The mean dermal exposure during application from a total of 12 replicates was 9.6 mg/lb. a.i., assuming the workers wore short-sleeved shirts, short pants, coveralls, waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear. The absorbed daily dosage for a worker loading and applying 1 lb. a.i. diquat during a day was calculated to be 2.4 ug/kg/workday (1.4% dermal absorption, body weight of 75.9 kg, and negligible inhalation exposure).

Chester, *et al*. (1989) monitored the exposure of Sri Lankan tea plantation workers using hand-operated or pressure retaining knapsack sprayers (4 gal. capacity). Paraquat was used at 0.26 lb. a.i./100 gal. at a rate 48 gal./acre. This is equivalent to an application rate of 0.12 lb/acre. Two workers mixed the concentrate formulation with water in large drums and loaded the solution into the knapsack tanks (equipped with double conejet nozzles) with buckets. The applicators (n=10) used the loaded knapsack sprayers to apply paraquat for spot treatment. All workers wore short-sleeved shirts and shorts. No gloves or footwear were worn, but workers exercised high standards of personal hygiene by washing hands, legs, feet, and contaminated skin frequently. Each applicator sprayed 7 to 8 knapsack tanks a day as a spot treatment in hilly and muddy conditions. The average amount of paraquat handled by an applicator was 33 g/day and by a mixer/loader was 164 g/day. The workers were all male with an average body weight of 49.3 kg.

Daily (24-hour) urine samples were collected the day before spraying started, during five days of spraying, and continued for 8 days after the last day of spraying. The workers did not have paraquat exposure at least two weeks prior to the start of this study. Blood samples were taken from workers to monitor serum concentration of paraquat. Blood samples were taken at the end of a workday on day 1, 3, and 5 of spraying days and the day after the last day of spraying. Urine and blood samples were stored frozen until shipment to the central laboratory for analysis. Blood and urine samples were analyzed for paraquat by ICI’s radioimmunoassay procedure CT05-085. The limit of detection for serum and urine were 0.006 and 0.03 ug paraquat ion/mL, respectively. Urine samples were also analyzed for creatinine to demonstrate completeness of 24-hour urine collection. The average daily urine volume was 1.94 liters.

No paraquat was detected in any of the serum or urine samples. Assuming that the urine samples contained paraquat at one-half the detection limit and based on the average daily urine volume of 1.94, average body weight of 49.3 kg, and 59 percent paraquat recovery in urine (Maibach, 1982), the ADD is calculated to be 1.0 ug/kg/day, as shown below:

[(0.015 ug/mL x 1940 mL) (100/59)]/49.3 kg = 1.0 ug/kg/day

In order to use the ADD for Sri Lankan tea plantation workers handling paraquat as surrogate to estimate an ADD for California workers handling diquat, the calculated ADD must be adjusted for the differences in dermal absorption rate, application rate (or dilution rate), number of tanks handled during a workday, and PPE worn during handling. The dermal absorption of diquat is estimated approximately three fold higher than that of paraquat. Diquat application rates of 0.5 lb/acre for agricultural uses and 0.5 to 1.0 lb/100 gal. for non-crop terrestrial uses are at least 4 fold higher than that in this study. Adjusting paraquat estimated ADD for diquat dermal absorption and application rates results in an ADD of 12 ug/kg/day. In addition, this study indicated that the number of tanks sprayed in a workday (7-8) in this hilly condition is two fold lower compared to 13 to 15 tanks handled in a workday in strip spraying in Malaysian plantations. Assuming that in California the number of tanks handled in a workday by a worker is the same as those of Malaysian plantations, the ADD was adjusted to 24 ug/kg/day for a worker wearing only a short-sleeved shirt and short pants.

It is apparent that the work practices conducted and the PPE worn by workers handling diquat in California will provide greater exposure protection compared to those used by the workers in this study. The level of protection provided by work practices can not be quantified. However, based on dermal exposure monitoring using dosimetry (conducted during this study), most of the exposure (99%) occurred to hands, legs, and trunk; therefore, we assume coveralls, gloves, socks, and shoes will provide 90 percent protection and reduce the estimated ADD to 2.4 ug/kg/day. Because of several assumptions and the multiplicative effects of each assumption on the estimate of ADD the inherent uncertainty with each assumption would also be multiplied. However, it is remarkable to note that the estimates of ADD based on these two studies (Chester *et al*., 1989 and Abbott, 1987) are identical.

Potential dermal exposure was also monitored during this study, but only during two replicates of spraying that took place on the day after the last day of urine monitoring. Each replicate consisted of the application of 4 tanks by each worker which lasted for approximately one hour. Mixer/loaders handled 113 g and applicators sprayed 22.7 g paraquat in a day. All workers wore Tyvek coveralls with hood, cotton gloves, and socks to monitor potential dermal exposure. The coveralls were cut in sections. These samples were stored and shipped at ambient temperature. Spike samples were taken to determine field recoveries of dosimeter samples.

Field recoveries at concentrations ranging between 0.01 and 0.03 mg/sample were 60, 67, and 95% for socks, gloves, and Tyvek, respectively. Field recoveries at concentrations ranging between 1.8 and 3.1 mg/sample were 119 to 122% for the same matrices. No corrections were made for field recoveries since the recoveries of samples spiked at concentrations close to the actual exposure were above 100%. Potential dermal exposure after handling 8 tanks (two replicates of 4 tanks each) was 66.1 mg/person for mixer/loaders and 73.7 $\pm$ 22.9 mg/person for applicators. Table 5 shows the estimate of exposure for workers applying diquat based on dermal monitoring of Sri Lankan tea plantation workers handling paraquat. The ADD based on dermal dosimetry exposure monitoring portion of this study overestimates exposure by three to four fold when compared to the estimates derived from the biomonitoring section of this study.

Table 5. Estimate of ADD for Workers Handling Diquat Using Knapsack Sprayers Based on the Exposure of Sri Lankan Tea Plantation Workers to Paraquat

	Mixer/loader exposure (n=2)		Applicator exposure (n=10)	
	mg/person	%	mg/person	%
head	0.1	0.2	0.9	1.2
trunk	2.8	4.2	3.5	4.7
arms	0.6	0.9	1.1	1.5
legs	1.7	2.5	22.3	30.3
feet	4.4	6.7	17.9	24.3
hands	56.5	85.5	27.9	37.9
Total potential	66.1	100	73.7	100
Total dermal[a]	61.5		49.4	
Total dermal[b]	6.2		4.9	
	ug/kg/day		ug/kg/day	
ADD[c]	1.1		0.9	
ADD[d]	9.1		7.2	

a - Short-sleeved shirt and sort pants, providing 90% protection to covered areas.
b - Coveralls (over short-sleeved shirt and short pants), waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear, providing 90% protection.
c - Based on dermal absorption of 1.4% (see dermal absorption section), and body weight of 75.9 kg.
d - Adjusted for 4 fold difference in dilution rate and 2 fold difference in the number of tanks handled in a workday.

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Right-of-Way Use

Diquat rights-of-way applications are primarily made by California Department of Transportation (Caltrans), county, and city employees using truck-mounted boom or hand-held sprayers. Worker Health and Safety Branch conducted a study to monitor the exposure to Caltrans employees applying herbicides to rights-of-way (Edmiston *et al*., 1994). The exposure data from this study for workers handling glyphosate was used as surrogate to estimate the exposure of workers handling diquat. Workers wore Tyvek coveralls and gloves over their normal clothing during mixing/loading and application of glyphosate. Dermal dosimeters (T-shirt and long underwear) were worn under normal clothing to estimate body dermal exposure. Face, neck, and hand wipes were used to estimate face, neck, and hand exposures. Applications were made from a truck using a hand sprayer connected to the spray truck. Table 6 shows glyphosate (anion) dermal exposure to workers performing various work activities. Samples with non-detectable levels were assumed to contain residues at one-half of the detection limit. Glyphosate was at the detectable levels only in two air samples taken from the breathing zone of workers. The method of application for diquat is similar to that of glyphosate. Using glyphosate data as surrogate, the estimates of ADD for workers applying diquat to rights-of-way range between 0.1 to 0.4 ug/kg/day, as shown in Table 6.

Table 6. Estimates of ADD for Workers handling Diquat Based on Dermal Exposure of Rights-of-Way Workers to Glyphosate

Work Task (n)	Head (ug/person)	Hand (ug/person)	body (ug/person)	Total[a] (ug/person)	ADD[b] (ug/kg/day)
Boom application (3)	350	744	134	1229 ± 876	0.23
Mix/load/hand wand application (12)	386	1015	846	2247 ± 1062	0.41
Driver/handling hose (3)	43	260	414	717 ± 310	0.13

n - Number of replicates.
a - Mean (arithmetic) ± standard deviation.
b - Assuming 1.4% dermal absorption, body weight of 75.9 kg, and negligible inhalation exposure.
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Drift

A diquat drift monitoring study, performed in Davis, California, showed residues on the fallout sheet and the air samples at downwind collection stations as far as 1,600 meters from the application site (Akesson, 1986). Diquat was sprayed from a height of five feet using a Weatherly 210 type aircraft at a speed of 100 to 110 miles/hour. The air sampling data were not defined adequately to estimate bystander's inhalation exposure to diquat, but the similarity of drift pattern between diquat and paraquat was evident. Paraquat drift data indicated air residues of 16.7 ug/m^3 and 0.5 ug/m^3 at 50 meters and 1600 meters respectively downwind of an aerial application at a rate of 0.18 lb. a.i./acre (Chester et al. 1981). Aerial applications move quickly across the fields, thus changing the distance of drift. In addition, a bystander is not expected to remain in a same area for more than two hours. Using paraquat drift data, bystanders' ADDs at various distances downwind from an aerial application of diquat were estimated as shown in Table 7.

Table 7. Estimates of Diquat Exposure to Bystanders Based on Paraquat Downwind Drift Study

Distance meter	Observed ug/m^3	Observed ug/m^3	Average ug/m^3	Calculated[a] ug/m^3	Corrected[b] ug/m^3	ADD[c] ug/kg/day
	trial I	trial II				
50	6.40	16.66	11.53	8.60	21.50	0.48
100	2.68	12.91	7.80	8.00	20.00	0.44
200	2.10			7.00	17.50	0.39
400	0.81	5.85	3.33	5.35	13.37	0.30
800	3.44	4.03	3.74	3.13	7.83	0.17
1600	1.70	0.47	1.09	1.07	2.68	0.06

a - from log linear correlation [ln y=2.214-0.0013x] where x is distance and y is the calculated residues in the air, r^2=0.895
b - corrected for 0.5 lb a.i.(from 0.2 lb/acre) and based on the previous column of calculated values.
c - inhalation rate of 0.84 m^3/hour (14 liters/minute) for light activity, body weight of 75.9 kg (Thongsinthusak, *et al.*, 1993), and daily two hours of exposure.
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Aquatic Dissipation
Aquatic dissipation of diquat was studied at two locations in Florida. Diquat was used at a rate of 4 lb. a.i./acre as surface treatment (Fujie, 1988). Four applications were made at each location at 30-day intervals. The ponds had no or very little outflow. Water samples were taken from top, middle and bottom of the pond. Water and sediment samples were taken prior to the first application and continued for about 30 days after each application. After the fourth application, sediment sampling continued for 180 days. Sample analysis indicated that diquat was distributed in all depths one day after application. Diquat dissipated rapidly from the water at both locations. Diquat concentration in water eight hours after the application ranged from 0.06 to 0.12 ug/mL. The concentration dropped to a range of 0.02 to 0.09 ug/mL 24 hours after the application and to a range of <0.004 to 0.02 ug/mL seven days after the application. The half-life at both sites ranged from 0.7 to 2.3 days (r = 0.96-0.99) with an arithmetic mean of 1.2 days. Sediment data reflected high variability. Samples taken 180 days after the last application showed little or no degradation from the levels found at seven days after the last application, indicating strong binding of diquat to the clay.

Diquat exposure to a swimmer from treated water is estimated based on a maximum application rate of 4 lb. a.i./acre foot (1.5 ppm). Dermal and ingestion are the primary routes of exposure. The reentry interval to treated water for swimming is 24 hours. In most dermal absorption studies (both *in vivo* and *in vitro*) a volume of 0.1 mL is applied to a skin area of one cm^2 as an ideal dermal exposure for a period of 24 hours (Corrigan, 1989a, b; Feldmann, 1974). This rate is equivalent to a thin film of the solution covering the skin area. Dermal exposure to diquat during swimming in treated water is comparable to the ideal 0.1 mL/cm^2 dermal exposure accommodated for dermal absorption studies. At this rate, the dermal exposure to a 75.9-kg male human with a skin surface area of 19,400 cm^2 (Thongsinthusak et al., 1993) is 1,940 mL of treated water.

Two scenarios were used to estimate diquat exposure to a swimmer spending four hours a day in the treated water. The first scenario assumes the theoretical maximum concentration of 1.5 ppm reached immediately following diquat application and this initial concentration drops to 0.75 ppm at its half-life of 1.2 days after the application. The second scenario is based on the actual measured concentration of 0.09 ppm in the water that was observed in the above dissipation study 24 hours following the application. Absorbed daily dosages (ADD) from dermal and oral routes for the above two scenarios are shown in Table 8.

Table 8. Estimate of Diquat Exposure to Swimmers from Treated Water

Scenario #	Concentration at reentry ug/mL	Water volume available for dermal exposure mL/person	Dermal exposure ug/person	Oral exposure ug/person	ADD ug/kg/day
1	0.75	1940	1455	75	1.26
2	0.09	1940	175	9	0.15

Based on: Dermal absorption rate of 1.4%, ingestion of 100 mL of treated water, body weight of 75.9 kg and four hours of exposure/day.

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Table 9. Diquat Workers Estimated Annual and Lifetime Average Daily Dosage

Work Task	Use	ADD (ug/kg/day)	AADD[a] (ug/kg/day)	LADD[b] (ug/kg/day)
Mixer/loader/applicator[c]	Ground	0.3	0.01	0.007
Flagger	Aerial	2.8	0.08	0.044
Pilot[d]	Aerial	0.3	0.01	0.005
Mixer/loader[e]	Aerial/Ground	7.8	0.21	0.122
Applicator (Ready-to-use)[d]	Garden/Landscape	0.4	0.02	0.009
Applicator (Knapsack)	Garden/Landscape	2.4	0.10	0.056
Applicator (hand sprayer)[f]	Right-of-way	0.1 - 0.4	0.007	0.004
Applicator (handgun)	Aquatic	0.5	0.01	0.008
Boat Driver (handgun)	Aquatic	0.1	0.003	0.002
Applicator (injection)	Aquatic	0.03	0.001	0.001
Mixer (injection)	Aquatic	0.06	0.002	0.001
Swimmer (theoretical)[g]	Aquatic	1.3	0.007	0.004
Swimmer (actual)[g]	Aquatic	0.2	0.001	0.001
Bystander(50 meters)	Aerial	0.5	0.014	0.008

Except as noted, the ADD values are estimated based on the product label highest rate of application and clothing consisting of short-sleeved shirt and short pants, coveralls, waterproof gloves, chemical resistant footwear and socks, protective eyewear, and chemical resistant headgear. The ADD for the bystanders is from the inhalation route for two hours of exposure/day.

a) Based on estimated diquat yearly exposure of 15 days for ground workers including garden/landscape, 10 days for aerial and aquatic workers (Ibarra, 1992; Mukai, 1992), 6 days for right-of-way workers (Haskell, 1994), and 2 days for swimmers.
b) A 40-year work period in a lifetime.
c) Long-sleeved shirt, long pants, headgear, footwear, and eyewear.
d) Long-sleeved shirt, long pants, and footwear.
e) The application rate and clothing protection were not provided.
f) Normal clothing, Tyvek coveralls, gloves, and footwear were worn during mixing/loading/application.
g) No clothing.

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