Glyphosate Biomonitoring for Farmers and Their Families: Results from the Farm Family Exposure Study

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Glyphosate is the active ingredient in Roundup agricultural herbicides and other herbicide formulations that are widely used for agricultural, forestry, and residential weed control. As part of the Farm Family Exposure Study, we evaluated urinary glyphosate concentrations for 48 farmers, their spouses, and their 79 children (4–18 years of age). We evaluated 24-hr composite urine samples for each family member the day before, the day of, and for 3 days after a glyphosate application. Sixty percent of farmers had detectable levels of glyphosate in their urine on the day of application. The geometric mean (GM) concentration was 3 ppb, the maximum value was 233 ppb, and the highest estimated systemic dose was 0.004 mg/kg. Farmers who did not use rubber gloves had higher GM urinary concentrations than did other farmers (10 ppb vs. 2.0 ppb). For spouses, 4% had detectable levels in their urine on the day of application. Their maximum value was 3 ppb. For children, 12% had detectable glyphosate in their urine on the day of application, with a maximum concentration of 29 ppb. All but one of the children with detectable concentrations had helped with the application or were present during herbicide mixing, loading, or application. None of the systemic doses estimated in this study approached the U.S. Environmental Protection Agency reference dose for glyphosate of 2 mg/kg/day. Nonetheless, it is advisable to minimize exposure to pesticides, and this study did identify specific practices that could be modified to reduce the potential for exposure. *Key words:* biomonitoring, epidemiologic studies, glyphosate, pesticide exposure. *Environ Health Perspect* 112:321–326 (2004). doi:10.1289/ehp.6667 available via *http://dx.doi.org/* [Online 3 December 2003]

Glyphosate [*N*-(phosphonomethyl)glycine] is the active ingredient in the Roundup (Monsanto Company, St. Louis, MO) brand of agricultural herbicides and in a variety of other herbicide formulations. These formulations provide nonselective, postemergent control of annual and perennial weeds and are used widely in agricultural, forestry, and residential markets. According to figures for 1999 [U.S. Environmental Protection Agency (EPA) 2002], glyphosate was second among pesticides in pounds applied in U.S. agriculture, and its use has been increasing with the rapid growth of acres planted with glyphosate-tolerant crops. Glyphosate has low oral acute mammalian toxicity [lethal dose for 50% of test animals (LD_{50}) > 5,000 mg/kg], and regulatory agencies and expert scientific bodies have concluded that it is not a mutagen, carcinogen, teratogen, or reproductive or developmental toxicant [U.S. EPA 1993; World Health Organization (WHO) 1994].

Herein, we present the glyphosate results from the Farm Family Exposure Study (FFES), a biomonitoring study of farmers and their spouses and children. The purpose of the FFES is to quantify real-world pesticide exposures immediately before, during, and after a pesticide application and to identify significant exposure determinants. The latter is important for developing valid exposure assessment approaches for epidemiologic studies and educational programs to help farm families minimize pesticide exposures.

Materials and Methods

Subject selection. We recruited farm families by randomly selecting licensed pesticide applicators from state listings in South Carolina and Minnesota. An initial solicitation letter was sent to applicators, followed a week later by a telephone call from a trained interviewer to assess eligibility and interest in participating in the study. Applicators could call a toll-free phone number supplied in the solicitation letter if they did not want to be contacted. From among those willing to be contacted, we selected families who met the following eligibility criteria: First, the farmer, spouse, and at least one child, 4–18 years of age, had to live on the farm. Second, they had to farm at least 10 acres within 1 mile of the family residence, to which they planned to apply one or a combination of the pesticides included in the study: glyphosate, 2,4-D (2,4-dichlorophenoxyacetic acid), or chlorpyrifos. There were no restrictions on using these pesticides before or immediately after the planned on-study application. Third, family members had to be willing to collect all urine voids for 5 consecutive days: the day before, the day of, and 3 days after the planned pesticide application. Finally, the farmer and spouse had to be willing to fill out pre- and poststudy questionnaires, thereby detailing family activities for the week before the study and the week of the study, and agree to have their on-study pesticide application observed by trained field staff. If all these conditions were met, an informed consent visit was arranged and the appropriate consent forms were signed to enable use of the resulting data for research purposes. The Institutional Review Board of the University of Minnesota approved the study protocol.

Participating families were given a cash incentive of $300 and reimbursed for the pesticide used during the on-study application to a maximum of $1,000. The average reimbursement for pesticides was approximately $700.

Urine collection and preparation of composite samples. Forty-eight farm families, including 79 children, provided specimens relating to a glyphosate application. During the study period, defined as 24 hr before the start of on-study pesticide-related activities (day –1) and continuing for 4 consecutive 24-hr periods (days 0, 1, 2, and 3, respectively), participants collected individual urine voids in 500-mL high-density polyethylene wide-mouth containers. Participants labeled these containers according to the date and time of each sample collection and stored them in coolers with blue ice packs (in South Carolina) or in mini-refrigerators (in Minnesota). Field research staff collected the samples daily, monitored compliance, logged each urine sample in a computer database, and created 24-hr composite urine samples with amounts proportional to the volume of each individual urine sample. Three composite samples (one 200-mL sample and two 100-mL samples) were frozen and shipped to a central coordinating center before one 100-mL sample was shipped to the analytic laboratory for analysis.

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Field staff also observed the designated pesticide application to document meteorologic conditions, work practices, and family activity patterns that might influence exposure potential.

We analyzed urine samples for creatinine to assess the completeness of daily samples. For farmers, the numbers of values below the normal range of 0.8–1.4 mg/dL (National Institutes of Health 2003) were 3, 2, 1, 2, and 3 for days –1 through 3, respectively. Using a normal range of 0.5–1.1 mg/dL for females, the numbers of subnormal values for days –1 through 3 were 2, 3, 2, 4, and 2, respectively. In the absence of reliable normative data by age for children, there is no accepted basis to estimate the number of subnormal creatinine values for FFES children.

Glyphosate analytic method. Pharmacokinetic research indicates that absorbed glyphosate is excreted unchanged, predominantly in urine (Williams et al. 2000). Urine samples were analyzed for glyphosate concentration at Monsanto's Environmental Sciences Laboratory (St. Louis, MO) using a previously published method (Cowell et al. 1986) modified for urine (FFES 2003). The method employs chelation ion exchange for the concentration and isolation of glyphosate, followed by quantitation using high-performance liquid chromatography with postcolumn reaction and fluorescence detection. The method has a limit of detection (LOD) of 1 µg/L (or 1 ppb) for a 100-mL urine sample.

The glyphosate results presented herein are corrected for laboratory analytical recovery and storage stability as determined by analysis of fortified field samples prepared throughout the study. Average overall recoveries for glyphosate were 69% for samples fortified at 10 ppb and 78% for samples fortified at 100 ppb.

Statistical methods. We calculated geometric mean (GM) urinary concentrations for farmer-applicators as the antilog of the average of the natural log (ln)–transformed urinary concentrations (SAS, version 8.2 for Windows; SAS Institute Inc., Cary, NC). The standard deviation (SD) was calculated as the antilog of the SD of the ln-transformed urinary concentrations. In these calculations, we assigned a value of 0.5 ppb (LOD/2) for concentrations that were below the LOD. We did not calculate GM concentrations for spouses and children because too few of these subjects had detectable concentrations in their urine.

We used t-tests and one-way analysis of variance to compare GMs for farmers who followed different application practices (SAS, version 8.2; SAS Institute, Inc.). We used two-tailed significance tests consistent with the null hypothesis of no relationship between application practices and urinary pesticide concentration.

Calculation of systemic dose. Systemic dose is an integrated measure of the amount of a substance absorbed per kilogram of body weight that provides a basis to compare human exposures with levels of toxicologic significance. We estimated systemic dose for all farmers, and for all spouses and children who had detectable urinary levels of glyphosate, by calculating the amount of glyphosate excreted during the study period, adjusting for incomplete excretion, adjusting for pharmacokinetic recovery, and dividing the total corrected excretion by each individual's body weight, as described below.

Calculating the amount excreted during the study period. The amount of glyphosate excreted each day during the study is equal to the daily urine concentration, corrected for field and laboratory recovery, multiplied by the daily urine volume. For example, a 10-ppb urine concentration and a daily urine volume of 2 L would equal a glyphosate excretion of 20 µg (i.e., 10 µg/kg × 2 kg; assuming specific gravity equal to 1 g/mL, then 1 L equals 1 kg). We calculated the total amount of glyphosate excreted during the study period (S_0) as the sum of the amounts excreted on days 0 through 3.

Adjusting for incomplete excretion. To estimate each individual's excretion rate during the study, a useful assumption is to consider S_0 to be the amount of glyphosate that is systemically available for excretion at the start of day 0. Likewise, the residual amounts that could have been excreted on days 1 through 3 equal S_0 minus the amount excreted before that particular day. Using this convention, we estimated each individual's excretion rate (k) based on an open, single-compartment pharmacokinetic model as the slope of the regression line of the logarithm of the daily residual amounts (over days 0 through 3) versus time. The fraction of S_0 that remains to be excreted after the last day of urine collection is then estimated for each individual from the equation $F = e^{-kt}$, where k is the individual's excretion rate (multiplied by 2.303 to translate a base-10 logarithm to a natural logarithm) and t is 4 days. We divided S_0 by $(1 - F)$ to estimate the amount of glyphosate that would have been excreted (S_1) had we collected urine until all of an individual's systemically available glyphosate was excreted.

Correcting for pharmacokinetic recovery. Wester et al. (1991) conducted a pharmacokinetic study of glyphosate with monkeys using intravenous dosing and were able to recover approximately 95% of the administered glyphosate. We divided S_1 by 0.95 to estimate of the amount of glyphosate that would have been recovered in urine with complete pharmacokinetic recovery (S_2).

Dividing the total estimated excretion by each individual's body weight. We divided S_2 by each individual's body weight to yield a systemic dose in milligrams per kilogram body weight.

Fourteen farmers made glyphosate applications after their on-study application, during the days of postapplication urine collection. We did not correct estimates of systemic dose in these instances so as to have the most conservative assessment of dose from the on-study applications. The contribution to systemic dose in all instances would be small.

Results

Table 1 details selected characteristics of participating farmers and spouses based on information reported in their enrollment and follow-up questionnaires. Farmers' and spouses' average ages were 45 and 42.2 years, respectively. Most farmers had spent their entire lifetimes living on a farm and had used pesticides an average of 23.9 years. About 15% of farmers and spouses reported being cigarette smokers. Few spouses reported that they had personally mixed pesticides.

Table 1. Characteristics reported by farmers and spouses on the enrollment and follow-up questionnaires.

	Farmers	Spouses
	No. (%)	No. (%)
Total number of farms	48	48
Minnesota	25	25
South Carolina	23	23
Average age (years)	45.0	42.2
Average years lived on farm	40.8	26.4
Average years applied pesticides	23.9	—
Additional job		
Yes	20 (41.7)	35 (72.9)
No	28 (58.3)	13 (27.1)
Currently smoke cigarettes		
Yes	7 (14.6)	7 (14.6)
No	40 (83.3)	41 (85.4)
No answer	1 (2.1)	
Schooling		
High school or less	19 (39.6)	20 (41.7)
Vocational school	12 (25.0)	6 (12.5)
Some college	4 (8.3)	7 (14.6)
College or graduate degree	12 (25.0)	13 (27.1)
Other		2 (4.2)
No answer	1 (2.1)	
Applied glyphosate in last 7 days before study		
Yes	14 (29.2)	
No	34 (70.8)	
Applied glyphosate within 3 days after on-study application		
Yes	14 (29.2)	
No	34 (70.8)	
Enclosed cab		
Yes	29 (60.4)	
No	19 (39.6)	
Glove changes		
Do not wear	10 (20.8)	
Change 1–4 times per season	13 (27.1)	
Change when worn out	12 (25.0)	
Change each time	5 (10.4)	
Change once a month	5 (10.4)	
Other	3 (6.3)	
Spouse personally mixed any pesticides in week before study		
Yes		2 (4.2)
No		46 (95.8)

The enrollment and follow-up questionnaires addressed a number of characteristics that might affect exposure. Twenty-two percent of farmers reported never wearing gloves when working with pesticides. Twenty-nine percent had applied glyphosate within a week before their scheduled on-study application. The same percentage made another glyphosate application within 3 days of their on-study application. Most farmers reported having tractors with enclosed cabins.

On the day of the on-study glyphosate application, a trained observer was present at each farm documenting practices and conditions that can influence exposure potential (Table 2). Twenty-nine percent of farmers were not wearing rubber gloves during their application. Gloves are not required when handling the glyphosate formulations used in this study, but use of rubber gloves when handling pesticides reduces dermal contact and systemic absorption. All the farmers used tractors and boom sprayers, and most applied the Roundup Ultra formulation (Monsanto Company) over glyphosate-tolerant crops early in the growing season. Skin contact with the glyphosate formulation was observed for 31% of farmers, and approximately 15% of farmers were observed to have had spills during mixing and loading or application. Twenty-seven percent repaired their equipment at some time during the application.

Urine concentrations of glyphosate for farmers ranged from < 1 ppb LOD to 233 ppb (Table 3). Some farmers did not have detectable glyphosate in their urine samples, despite applications in excess of 100 acres. Overall, the percentage with detectable values was 60% on the application day, declining to 27% by day 3. The GM for farmers was 3.2 ppb on the application day and declined thereafter. Findings differed between South Carolina and Minnesota. On the application day, 87% of the South Carolina farmers had detectable values, compared with 36% of the Minnesota farmers. Geometric mean values were 7.9 ppb in South Carolina and 1.4 ppb in Minnesota (Table 4).

Urinary concentrations were appreciably lower for farmers who were observed to wear rubber gloves when mixing and loading glyphosate formulations (Table 4). The GM for those wearing rubber gloves was 2.0 ppb versus 9.7 ppb for other farmers. Values above the LOD were less common for those who wore rubber gloves (50%) than for those who did not (86%). Use of rubber gloves was much more common in Minnesota (96%) than in South Carolina (43%). The number of acres treated was not correlated with urinary glyphosate concentration, but there was a trend between concentration and the number of times farmers mixed and loaded the concentrated herbicide formulation. Other factors associated with urinary concentration were using an open cab tractor, observed skin contact with the glyphosate formulation, and repairing equipment during the application. Using a closed transfer system was not associated with lower urinary values.

Table 5 presents factors that might influence urinary concentrations stratified by use of rubber gloves. These factors were associated with small differences in average urinary values for farmers who used gloves. In contrast, for farmers who did not wear gloves, the number of acres treated, the number of mixing/loading operations, observed spills, and repairing equipment were associated with appreciable differences in average urinary values.

Detectable values were infrequent for farm spouses and children (Table 3). Two of 48 spouses (4%) had detectable values on the day of application. The highest individual urinary concentration was 3 ppb. No spouse participated in the pesticide application. Eight spouses were observed to have been in the immediate vicinity at some time during mixing, loading, and application, but none had detectable urinary levels of glyphosate. There was no correlation between urinary levels for spouses and the number acres treated, presence in the field, or the distance between the house and the treated field. Forty spouses washed the farmers' application clothes during the study period. Two showed detectable levels of glyphosate in their urine—both 1 ppb on a single day—during the 3 days postapplication.

The average age of participating children was 11.5 years, and 54% were boys. Nine of 78 (12%) children who provided samples had a detectable value on the day of application. All were from farms in South Carolina (n = 38 children), and all but one were reported by their parents to have been present for or assisted with herbicide mixing or application activities. Only 1 of 52 children (2%) had a detectable value (1 ppb) on the day of application if they were not reported to have been present during mixing or application. Eight of 26 (31%) children had a detectable value in their urine if they were reported to have helped or been present for the pesticide mixing or application.

The maximum urinary concentration for a child, 29 ppb, was for a teenage boy who actively assisted his father with the mixing and application. The boy's father had the highest urinary concentration among applicators. The field notes documented long periods spent by

Table 2. Field observers' characterization of farmers on the day of application.

	No. (%)
Rubber glove use when mixing/loading	
Yes	34 (70.8)
No	14 (29.2)
Acres treated	
10–44	16 (33.3)
45–124	16 (33.3)
125–439	16 (33.3)
Number of loads	
1–2	12 (25.0)
3	15 (31.3)
4–6	12 (25.0)
7–12	9 (18.8)
Tractor with closed cab	
Yes	29 (60.4)
No	19 (39.6)
Pesticide spills during mixing	
Yes	7 (14.6)
No	41 (85.4)
Pesticide spills during applying	
Yes	8 (14.6)
No	40 (85.4)
Skin contact with pesticides	
Yes	15 (31.3)
No	33 (68.7)
Repaired equipment during application	
Yes	13 (27.1)
No	35 (72.9)

Table 3. Urinary glyphosate values for study participants.

	No. samples	> LOD[a] No. (%)	GM (SD)[b]	Range[b]
Farmer-applicators				
Preapplication	47	7 (15)	—[c]	< 1–15
Application day	48	29 (60)	3.2 (6.4)	< 1–233
Postapplication day 1	48	23 (48)	1.7 (4.6)	< 1–126
Postapplication day 2	48	16 (33)	1.1 (3.7)	< 1–81
Postapplication day 3	48	13 (27)	1.0 (3.6)	< 1–68
Spouses				
Preapplication	47	1 (2)	—	< 1–3
Application day	48	2 (4)	—	< 1–2
Postapplication day 1	48	0 (0)	—	All < 1
Postapplication day 2	48	1 (2)	—	< 1–1
Postapplication day 3	48	1 (2)	—	< 1–1
Children				
Preapplication	76	5 (7)	—	< 1–17
Application day	78	9 (12)	—	< 1–29
Postapplication day 1	78	7 (9)	—	< 1–24
Postapplication day 2	79	5 (6)	—	< 1–12
Postapplication day 3	75	4 (5)	—	< 1–6

[a]LOD is 1 ppb. [b]In parts per billion. [c]We did not calculate geometric means when < 25% had detectable values.

Table 4. Glyphosate urinary concentrations on the day of application according to field observers' observations.

	No.	GM[a]	SD[a]	Range[a]	*p*-Value
State					
Minnesota	25	1.4	5.2	< 1–66	
South Carolina	23	7.9	5.2	< 1–233	0.0006
Rubber glove use when mixing					
No	14	9.7	6.3	< 1–233	0.006
Yes	34	1.5	4.8	< 1–66	
No. of acres treated					
10–44	16	2.9	4.7	< 1–34	
45–124	16	2.9	8.4	< 1–233	
125–439	16	3.8	7.0	< 1–101	0.89
No. of loads					
1–2	12	1.2	3.9	< 1–19	
3	15	2.9	7.3	< 1–233	
4–6	12	3.8	4.9	< 1–34	
7–12	9	10.7	7.3	< 1–101	0.05
Closed cab					
No	19	6.5	6.7	< 1–233	0.03
Yes	29	2.0	5.4	< 1–101	
Observed spills during mixing/loading					
No	41	2.7	5.6	< 1–101	
Yes	7	7.3	12.2	< 1–233	0.20
Observed spills during application					
No	40	2.5	5.3	< 1–66	
Yes	8	9.2	11.3	< 1–233	0.07
Skin contact with pesticides					
No	33	2.0	5.1	< 1–51	
Yes	15	9.0	6.8	< 1–233	0.007
Repaired equipment during application					
No	35	2.3	5.6	< 1–66	
Yes	13	7.2	7.6	< 1–233	0.06
Closed system					
No	39	3.3	6.4	< 1–233	0.99
Yes	8	3.3	7.2	< 1–66	
Do not know	1	—	—	—	

[a]In parts per billion.

Table 5. Glyphosate urinary concentrations on the day of application according to use of rubber gloves and field observers' observations.

	Use of rubber gloves when mixing/loading					
	Yes			No		
	No.	GM[a]	SD[a]	No.	GM[a]	SD[a]
State						
Minnesota	24	1.4	5.3	1	—	—
South Carolina	10	4.5	4.3	13	12.2	5.5
No. of acres treated						
10–44	10	3.4	5.6	6	2.1	3.7
45–124	11	0.9	3.7	5	33.7	3.5
125–439	13	2.5	6.0	3	25.1	4.8
No. of loads						
1–2	8	0.8	3.6	4	2.5	3.9
3	11	1.8	5.0	4	10.6	13.4
4–6	9	2.6	5.0	3	11.4	2.6
7–12	6	5.1	7.7	3	45.8	2.3
Closed cab						
No	12	4.7	5.8	7	11.2	8.7
Yes	22	1.2	4.3	7	8.4	5.0
Observed spills during mixing/loading						
No	28	1.7	4.7	13	7.6	5.3
Yes	6	4.1	8.8	1	232.7	—
Observed spills during application						
No	28	1.7	5.0	12	6.1	4.6
Yes	6	3.6	7.2	2	153.6	1.8
Observed skin contact with pesticides						
No	27	1.5	4.7	6	6.8	4.7
Yes	7	6.2	6.0	8	12.6	8.1
Repair of equipment during application						
No	27	1.9	3.7	8	4.6	5.9
Yes	7	2.4	12.3	6	26.0	4.7
Closed system						
No	26	2.0	5.3	13	8.8	6.5
Yes	7	2.3	6.5	1	34.1	—

[a]In parts per billion.

the farmer repairing the boom sprayer and evidence of spills while mixing and loading. The use of protective gloves was not observed for father or son during mixing or loading or during the repairs. The father was also observed to smoke cigarettes while repairing the boom sprayer.

The maximum systemic dose for farmer-applicators was estimated to be 0.004 mg/kg, and the distribution of values was highly skewed (Figure 1). The GM systemic dose was 0.0001 mg/kg. For comparison, according to the U.S. Environmental Protection Agency (U.S. EPA), the lowest no effect level from glyphosate toxicology studies is considered to be 175 mg/kg/day, and the reference dose (an estimate of the daily oral exposure to the human population, including sensitive subgroups such as children, that is not likely to cause harmful effects during a lifetime) is 2 mg/kg/day (U.S. EPA 1993). Maximum systemic dose estimates for spouses and children were 0.00004 mg/kg and 0.0008 mg/kg, respectively.

Discussion

The results of this analysis provide a perspective on the amount of glyphosate absorbed by farmers and their family members around the time of a glyphosate application. Exposure potential appears to be especially limited for those not present in the immediate area of mixing, loading, or application activities. Even among farmers, 40% did not have detectable levels in their urine on the day of application. The highest values for farmers were most clearly associated with not wearing rubber gloves when handling the pesticide formulation. For children, it appeared that most detectable exposures could have been prevented or minimized by avoiding the immediate vicinity during pesticide mixing or application. In all instances, systemic dose estimates were well below the U.S. EPA's reference dose for glyphosate.

The exposure patterns we observed for glyphosate are consistent with its physicochemical properties. The vapor pressure of glyphosate is extremely low. Glyphosate is usually formulated as the isopropylamine salt, which has a vapor pressure of 1.6×10^{-8} mm Hg (Tomlin 2000). Inhalation of spray droplets was found to be a minor route of glyphosate exposure in a study in Finland (Jauhiainen et al. 1991), leaving dermal contact as the primary route of exposure. Glyphosate is soluble in water and has low affinity for organic materials such as skin. Dermal penetration experiments, where glyphosate was left undisturbed on skin surfaces of experimental animals and on human skin *in vitro*, indicate a percutaneous absorption of less than 2% (Wester et al. 1991). The experimental conditions for the skin penetration studies were developed to maximize absorption, so actual human percutaneous absorption may be less.

Our results for farmers are consistent with biomonitoring studies performed on silvicultural workers. In a study conducted by researchers at the Georgia Institute of Technology and Monsanto Company, investigators assessed the exposure of applicators during hand-held directed-spray foliar application of the original Roundup formulation at three sites maintained by the U.S. Department of Agriculture (USDA) Forestry Service (Cowell and Steinmetz 1990). Urine samples from 15 participants were collected for a period of 5 days—the day before, the day of, and the 3 days after the application. Urine specimens were combined to form 12-hr composite samples for each worker. Four of 15 workers had detectable levels of glyphosate in their urine samples from the day of application. There were no detectable values on other days. The highest individual glyphosate measurement was 14 ppb, and the highest estimated systemic dose was 0.0006 mg/kg body weight. The LOD for that study was 10 ppb (Cowell and Steinmetz 1990).

Researchers from the University of Arkansas and Monsanto conducted a USDA-sponsored silvicultural study of workers at two forestry nurseries (Lavy et al. 1992). The study included three applicators who applied the original Roundup formulation to weed-infested areas near the nurseries and to fallow nursery beds. These applicators collected all their urine the day before an application and for 5 days starting the day of application. Nine weeders also included in the study made spot glyphosate applications intermittently from May through August. Twenty-four–hour urine samples were collected daily for 12 weeks and pooled over 3 or 4 days to provide two pooled samples per week for each weeder. None of the urine samples in this study was found to have quantifiable levels of glyphosate based on a 10 ppb LOD.

A number of limitations need to be considered when interpreting our results. First, we evaluated only one application per family, so our results may not encompass the variation in exposure over a season or over years of applications. This potential limitation can only be addressed by repeated sampling of farm families. Second, a tractor and boom sprayer were used for all of the glyphosate applications, so our results may not be representative of other application procedures. However, tractor and boom sprayer are the predominant equipment for applying glyphosate in agriculture, and our results are consistent with two studies where glyphosate was applied in forestry with hand sprayers (Cowell and Steinmetz 1990; Lavy et al. 1992). Third, it is possible that participation in the study influenced application practices. We tried to minimize this potential bias by employing experienced field staff to interact with study participants and by instructing staff not to interfere with farm activities. The proportion of FFES applicators using rubber gloves (43% in South Carolina and 96% in Minnesota) is similar to that reported from the Agricultural Health Study (39% in North Carolina and 76% in Iowa; Alavanja et al. 1999), so use of personal protective equipment in our study seems typical. Finally, our study protocol required extensive collection of urine samples and therefore may be more subject than other biomonitoring studies to selection bias. Of farmers we contacted, 12% of those who were eligible declined to participate, and a number who were willing to participate could not be scheduled before we met our quota for glyphosate farms. We did not find appreciable differences on demographic factors for eligible participants and nonparticipants. Nonetheless, selection bias could be operative, and it is unclear whether such a bias would include higher or lower exposure farm families in our study. The similarity between FFES farmers and those in other studies with respect to smoking prevalence (Alavanja et al. 1996) and glove use (Alavanja et al. 1999) would suggest that our study participants were a fairly typical sample of the population of farm families with young and teenage children.

As reported by Mandel et al. (In press) and Acquavella et al. (In press), the FFES findings for glyphosate were distinctly different from the FFES findings for 2,4-D and chlorpyrifos. Glyphosate was associated with fewer urinary detections among farmers and especially among spouses and children. In addition, for farmers, patterns of uptake and elimination appeared to be different for each pesticide, and urinary levels were markedly lower for glyphosate than for the other chemicals. This would suggest the importance of a chemical-specific approach to exposure assessment for epidemiologic studies or, perhaps, grouping pesticides that have similar physicochemical properties and application practices.

It is noteworthy that our assessment of systemic dose for applicators suggests a narrow range of systemic doses, including many that fell below modern analytic limits. For farmers who used rubber gloves, there were small variations in urinary concentration according to the number of acres treated, the number of mixing and loading operations, observed spills, or equipment repairs. On the other hand, we saw larger differences in these factors for farmers who did not use rubber gloves. However, the variation that did exist did not translate into appreciably different absorbed doses because 90% of all applicators had systemic doses below 0.001 mg/kg body weight.

An important rationale for the FFES was to collect data relevant to concerns about real-world exposures for farm spouses and children (Gladen et al. 1998). We found little evidence of detectable exposure for family members not involved in or in the immediate vicinity of glyphosate applications. Obviously, this bears consideration for epidemiologic studies that might assign glyphosate exposure for people who do not apply pesticides based solely on farm residence or residential proximity to an application for nonfarm residents.

The results of our analyses suggest that modifying specific practices should be effective in minimizing glyphosate exposures for farmers, spouses, and their children. For farmers, the use of rubber gloves when mixing and loading pesticides or when repairing equipment was associated with measurably reduced urinary concentrations. For children or spouses who are not directly involved in pesticide activities, taking care to avoid the immediate area for pesticide mixing, loading, or application is advisable. Although the systemic doses estimated in this study were well below the reference dose for glyphosate, it is advisable nonetheless to minimize pesticide exposure. In that context, our results provide empirical support for the types of practices that should be effective to minimize absorbed dose for glyphosate and for other pesticides that have similar physicochemical properties.

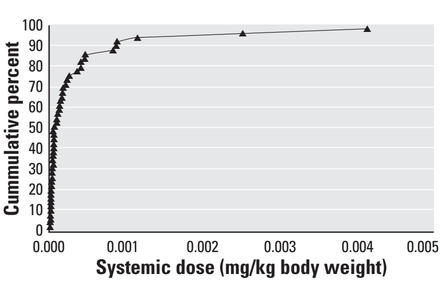

Figure 1. Cumulative percentage plot of glyphosate systemic doses for farmers.

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