

This is a Monsanto-produced summary of the following paper:

Safety Evaluation and Risk Assessment of the Herbicide Roundup and Its Active Ingredient, Glyphosate, for Humans  
by G.M. Williams, R. Kroes, and I.C. Munro, 2000  
*Regulatory Toxicology and Pharmacology* 31:117-165

Limited copies of the original 48-page paper available from VFM

## Backgrounder

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### Summary of Human Risk Assessment and Safety Evaluation on Glyphosate (and Roundup® Herbicide)

Three internationally recognized toxicologists have completed and published a peer-reviewed safety evaluation and risk assessment of glyphosate and the most commonly sold Roundup herbicide formulations. The authors (see biographical data below\*) reviewed Monsanto studies which had previously been reviewed by regulatory authorities around the world (see below).\*\* In addition, they reviewed regulatory and scientific organization reports as well as a wide array of studies conducted by independent researchers using information obtained from public literature. Over a two-year period, they examined and critiqued 188 documents to prepare a comprehensive evaluation of glyphosate.

The basic Roundup formulation that has been used around the world for 30 years contains the active ingredient glyphosate (in the form of its isopropylamine salt), water and a surfactant (POEA or polyethoxylated alkyl amine). For most agricultural and industrial uses, Roundup formulations contain 41 percent glyphosate isopropylamine salt and must be diluted with water before application. The ready-to-use product sold to homeowners contains a 1 percent solution of glyphosate isopropylamine salt. The reviewers conducted a risk assessment of the formulated product, the surfactant, the active ingredient and its major breakdown component, AMPA (aminomethyl phosphonic acid). They considered exposures during both application of the product and consumption of treated food crops.

The paper, "Safety Evaluation and Risk Assessment of the Herbicide Roundup and Its Active Ingredient, Glyphosate, for Humans," by Gary M. Williams, Robert Kroes, and Ian C. Munro, was published in *Regulatory Toxicology and Pharmacology*, (2000) Volume 31, pages 117-165.

Key findings of this study include:

- **Glyphosate is not a carcinogen.** – *"The chronic toxicity and oncogenic potential of glyphosate ... have been evaluated by a number of regulatory agencies and by international scientific organizations. Each of these groups has concluded that glyphosate is not carcinogenic."* (p. 126) This is based on long-term studies in which mice and rats were fed extremely high doses of glyphosate every day for two years. The U.S. EPA has placed glyphosate in Category E ("evidence of non-carcinogenicity for humans"), the most favorable carcinogenicity category possible.
- **Roundup has very low acute toxicity, which means very high exposure is required to cause an adverse effect.** The reviewers evaluated the potential short-term (acute) exposure and risk to herbicide applicators and children living on a farm. These two population groups have the maximal opportunity for exposure because they are most likely to come in contact with herbicide sprays and residues. In addition, children age 1 to 6 are assumed to have the highest dietary exposure because they eat more of some foods per body weight than other age groups. In the exposure assessment, it was assumed that the child occasionally enters a recently sprayed farm field and stays there for up to five hours, playing or helping a parent. The authors compared the acute oral LD50s of glyphosate and POEA to a calculated acute exposure to these two subgroups. (LD50 is a standard for expressing the toxicity of a compound.) The calculated acute exposure of the two subgroups in the on-farm study that have maximal assumed opportunity for exposure were estimated to be 40,000 to 50,000 times lower than the LD50 of glyphosate and 7,360 to 13,200 times lower than the LD50 of POEA. (p. 159-160) Other studies showed that serious effects occurred only when large amounts of concentrated Roundup (e.g. ≥ 41%) were intentionally ingested. (p. 149)

- Roundup poses minimal risk of injury.** *“Roundup is placed in U.S. EPA’s least toxic category (IV) for acute oral, dermal and inhalation toxicity. Thus, the Roundup formulation is considered to be practically nontoxic by all these routes of exposure. ... POEA is considered to be only slightly toxic and does not represent an acute toxicity hazard.”* (p. 129) *“Results from several investigations establish that the acute toxicity and irritation potential of Roundup herbicide in humans is low.”* (p. 148) With Roundup formulations containing the POEA surfactant, there is potential for eye irritation if the spray is misdirected or if splashing occurs during mixing with water. The surfactant POEA, in its concentrated form, is severely irritating to eyes, but the researchers reported that *“POEA is not used in concentrated form but rather is formulated at lower concentrations into an end-use product (Roundup) and later diluted to very low levels, rendering it significantly less irritating ... When diluted to a concentration commonly used for most spraying applications (~1%), Roundup was shown to be only minimally irritating to eyes and essentially non-irritating to skin.”* (p. 129) The researchers also addressed a statistic commonly cited by pesticide activist groups, which identify Roundup as a leading cause of pesticide illness in California. *“Careful examination of the California data further indicates that the number of cases reported simply reflects greater use of the product relative to other herbicides and shows that glyphosate has relatively low toxicity among pesticides used in the State ... In 1994, for example, glyphosate exposure was reported in only 25 cases, of which only 13 were considered “definite or probable.” Eleven of the 13 cases involved only minor and reversible eye irritation; the other two cases were a headache and an apparent misdiagnosis of reaction to hydrocarbon solvent, which is not an ingredient in Roundup.”* The researchers noted that the California Department of Pesticide Regulation, which compiles pesticide illness figures, noted in its 1994 report that the majority of people reporting Roundup exposure experienced only irritant effects and that in 13 years of record keeping, there had been no hospitalization linked to Roundup. (pp. 147-148)
- Glyphosate does not bioaccumulate.** *“The potential for systemic exposure is limited by the combination of poor absorption and rapid excretion of glyphosate after oral and/or dermal contact.”* (p. 124) As glyphosate is not stored in the body, any exposure from skin contact or inhalation would be quickly eliminated by humans and animals.
- Glyphosate does not adversely affect reproduction or development.** *“Results from several studies have established that glyphosate is not a reproductive or developmental toxicant.”* (p. 128) In developmental toxicity studies, and in multi-generation animal studies in which high doses were fed to laboratory animals, *“there were no effects on fertility or reproductive parameters, and glyphosate did not produce birth defects.”* (pp. 127-128) The developmental toxicity of the surfactant predominantly used in Roundup formulations worldwide (POEA) and its possible effects on the reproductive system have also been evaluated in animal studies. *“There is no evidence that the surfactant or Roundup herbicide adversely impacts reproductive function.”* (p. 131) The authors devoted several paragraphs to their critique of a rabbit study often cited by pesticide critics to imply sperm count reduction. (Yousef et al., 1995) *“There were a number of serious deficiencies in the design, conduct and reporting of this study which make the results uninterpretable. ... the data from this study cannot be used to support any meaningful conclusions.”* (p. 127-128)
- Children are not at greater risk.** *“The U.S. EPA has recently evaluated tolerance petitions under the Food Quality Protection Act of 1996 (FQPA) (Public Law 104-170) which includes special provisions to protect infants and children. The U.S. EPA concluded that there is “reasonable certainty” that no harm will occur from aggregate exposure to glyphosate (U.S. EPA 1997a, 1998a).”* (p. 128) EPA also concluded that the currently applied safety factor of 100 is adequate to protect children. *“There was no suggestion of increased severity of effect in infants or children or of increased potency or unusual toxic properties of glyphosate in infants and children.”* (p.156)
- There is no evidence of endocrine disruption.** *“The endocrine-modulating potential of glyphosate has been evaluated in a variety of studies including in vitro assays and standard in vivo toxicology studies. The in vivo studies comprehensively assess endocrine functions that are required for reproduction, development, and chronic health. Glyphosate produced no effects in in vitro assays, and there was no indication of changes in endocrine function in any of the in vivo studies. Results from standard studies with AMPA, Roundup herbicide, and the POEA surfactant also failed to show any effects indicative of endocrine modulation. Therefore, it is concluded that the use of Roundup herbicide has no potential to produce adverse effects on endocrine systems in humans nor in other mammals.”* (p.143)

- **There is no synergistic adverse effect.** Herbicides sometimes are applied in combination with other herbicides, raising the question of whether the combination creates a synergistic effect (more than an additive response). *"The toxicity of glyphosate has been evaluated in combination with several surfactants and/or other herbicides ... it is concluded that the simultaneous exposure of glyphosate and other materials does not produce a synergistic response."* (p. 145)

**REFERENCES IN ITALICS THROUGHOUT THIS DOCUMENT REFER TO STATEMENTS OR CONCEPTS EXPRESSED BY THE AUTHORS OF "SAFETY EVALUATION AND RISK ASSESSMENT OF THE HERBICIDE ROUNDUP AND ITS ACTIVE INGREDIENT, GLYPHOSATE, FOR HUMANS."**

**\*BIOGRAPHICAL DATA:**

**Gary M. Williams, M.D.**, is Director of Environmental Pathology and Toxicology and Head of the Program on Medicine, Food and Chemical Safety at New York Medical College, Valhalla, N.Y. He is a board-certified pathologist, physician and toxicologist in the United States and has also been certified as an Expert in Toxicology by the French Ministere des Affaires. He has served as an editor or editorial board member for more than 25 scientific journals and papers. Williams has also organized more than 20 scientific meetings and conferences around the world, many of which discussed safety assessments of pharmaceuticals and chemicals, and cancer screening tests and prevention.

**Robert Kroes, Ph.D.**, is the Director of the Research Institute for Toxicology at Universiteit Utrecht in The Netherlands. He is board-certified in toxicology and pathology and specializes in toxicology, oncology and risk assessments. He served for seven years as Deputy Director General of the Dutch National Institute of Public Health and Environmental Protection. He has served as a member of more than 20 international expert panels on toxicology, oncology and environment and health, including groups impaneled by the World Health Organization, the Food and Agriculture Organization of the United Nations, the Organization for Economic Cooperation and Development, and the European Union. He is an editorial board member of 13 scientific periodicals.

**Ian C. Munro, Ph.D.**, is President of CANTOX Health Sciences International and a professor in the Department of Nutritional Sciences at the University of Toronto, Ontario, Canada. He is a Fellow at The Academy of Toxicological Sciences and the Royal College of Pathologists in London. He has more than 150 scientific publications in the fields of toxicology and risk assessment. He formerly held senior positions at Health and Welfare Canada as Director of the Bureau of Chemical Safety and Director General of the Food Directorate, Health Protection Branch. He also was Director of the Canadian Centre for Toxicology at Guelph, Ontario. Munro has served on more than 30 expert panels, nationally and internationally, including those of the World Health Organization, the International Agency for Research on Cancer and the U.S. National Academy of Sciences, where he chairs a subcommittee. He is a recipient of the "International Achievement Award" of the International Society of Regulatory Toxicology and Pharmacology. He has served on the editorial boards of Neurotoxicology, the Journal of the American College of Toxicology, and the Journal of Environmental Pathology and Toxicology.

**\*\*** *"Government regulatory agencies in several countries, international organizations, and other scientific institutions and experts have reviewed the available scientific data and independently judged the safety of glyphosate and Roundup. Conclusions from three major health organizations [Health Canada, United States Environmental Protection Agency (U.S. EPA), and World Health Organization (WHO)] are publicly available (Health and Welfare Canada, 1986, 1992; U.S. EPA, 1993, 1997a, 1998a; WHO 1994a). Those reviews, which have applied internationally accepted methods, principles, and procedures in toxicology, have discovered no grounds to suggest concern for human health."* (pp. 118-119)

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