



Backgrounder

Glyphosate: Response to “Differential effects of glyphosate and Roundup on human placental cells and aromatase”

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Monsanto Company

In March 2005, Pr. Gilles-Eric Seralini’s group in the University of Caen (Normandy, France) published the results of a study examining the effect of Roundup and glyphosate on cultured cells derived from a human placental cancer (choriocarcinoma) (Richard *et al.*, 2005).

The authors imply that Roundup (see Note) is an endocrine disruptor based on effects in human tumor cells originally derived from a cancer of the placenta. Aromatase activity, which is required for the production of certain steroid hormones, was decreased when these tumor cells were exposed to high concentrations of Roundup in a Petri dish for 18 hours.

The study, while interesting, has no relevance to a living animal. The implications of this *in vitro* experiment are contradicted by extensive live animal data and field studies reflecting real-world conditions.

The cells used in this study were taken from a human placental tumor, put into a Petri dish, and covered with culture media containing Roundup or other test materials. This direct exposure to high concentrations is vastly different than what would occur in a human or animal body, i.e. - the concentration of Roundup reported to have caused a reduction in aromatase activity was orders of magnitude greater than would result from the highest possible human exposure under real conditions. The direct exposure used in this study intentionally bypasses normal processes limiting absorption and cellular exposure and avoids normal metabolism, digestion and excretion that would protect cells from the minute amounts of chemical.

These cell lines are used as mechanistic research tools and are not recognized or accepted by any regulatory agency or other scientific body in the world for the assessment of human health risks.

Glyphosate has been tested extensively in higher order animals (Giesy *et al.* 2000; Williams *et al.* 2000). There is no evidence for developmental or reproductive effects in multiple species despite numerous high-dose tests by different manufacturers (EU, 2002). Furthermore, studies with surfactants in Roundup agricultural herbicides have demonstrated no target organ toxicity or effects on the embryos, fetus, or placenta (Williams *et al.* 2000).

Walsh *et al.* (2000) previously suggested that Roundup had endocrine disruption potential based on decrease in progesterone synthesis in mouse Leydig tumor cells exposed to supra-physiologic concentrations of formulated herbicide in a Petri dish. Monsanto and an academic collaborator (Levine *et al.* 2003; Heydens *et al.* 2003) repeated this experiment with the inclusion of a sensitive cytotoxicity assay that assessed mitochondrial membrane damage. This experiment demonstrated that decreased progesterone synthesis resulted from surfactant-induced

Note: The Roundup® product line consists of multiple agricultural and residential use products with varying ingredients and concentrations. Richard *et al.* have not specified the product or formulation used in their research. The term Roundup is used herein to refer generally to Roundup agricultural herbicides having glyphosate as their active ingredient.

mitochondrial membrane damage. In separate follow-up experiments, a number of surfactants commonly found in household products were tested. Each of these surfactants produced concentration-dependent decreases in progesterone synthesis and cytotoxicity comparable to that observed with concentrated Roundup formulation when tested in these mouse tumor cells. The results of these studies underscore: (1) the non-specific action of a variety of surfactants on cellular function in an *in vitro* test system; and (2) how this secondary activity can confound the results when surface-active agents are used in *in vitro* test systems.

Based on estimates of human exposure to Roundup herbicides from agricultural and residential uses by various routes, and based upon the non-specific metabolic effects of surfactants on tumor cells in Petri dishes, it is apparent that Roundup will not disrupt steroid synthesis *in vivo* under biologically relevant conditions.

References:

- EU (European Union). (2002) Review report for the active substance glyphosate. http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1_glyphosate_en.pdf.
- Giesy JP, Dobson S, Solomon KR. (2000) Ecotoxicological risk assessment for Roundup herbicide. *Reviews of Environmental Contamination and Toxicology* 167: 35-120.
- Heydens WF, Levine SL, Farmer DR, Han Z, Wall C, Papadopoulos V. (2003) Non-specific alteration of steroidogenesis in MA-10 Leydig cells by supra-physiological concentrations of the surfactant in Roundup herbicide. *Toxicologist*, 131.
- Levine SL, Farmer DR, Heydens WF, Han Z, Wall C, Papadopoulos V. (2003) Non-specific alteration of steroidogenesis *in vitro* by supra-physiological levels of surfactant. Society of Environmental Toxicology and Chemistry, 22nd Annual Meeting Abstracts.
- Richard S, Moslemi S, Sipahutar H, Benachour N, Seralini GE. (2005) Differential effects of glyphosate and Roundup on human placental cells and aromatase. *Environmental Health Perspectives* (in press).
- Walsh LP, McCormick C, Martin C, Stocco DM. (2000) Roundup Inhibits Steroidogenesis by Disrupting Steroidogenic Acute Regulatory (StAR) Protein Expression. *Environmental Health Perspectives* 108(8): 769-776.
- Williams GM, Kroes R, Munro IC. (2000) Safety Evaluation and Risk Assessment of the Herbicide Roundup and its Active Ingredient, Glyphosate, for Humans. *Regulatory Toxicology and Pharmacology* 31: 117-165.

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