The article by Paganelli et al. (Chem. Res. Toxicol. (2010), 23, 1586–1595) is seriously flawed in terms of the experimental designs, the lack of clear descriptions of the methods used, the interpretation of the results, and in the extrapolation of the responses observed in the eggs of frogs and chickens to humans. The more egregious errors in the article are discussed below, but the article was also lacking in details of the methods as well as rigorous use of statistical tests, such as regression analysis of the concentration responses.

In the first part of the study on embryos of *Xenopus laevis*, exposures to the formulated product (Roundup Classic; 480 g/glyphosate IPA salt/L) at 1/3000; 1/4000; and 1/5000 dilutions were equivalent to 71,158; 88,947; and 118,596 μg a.e./L, respectively. The concentrations are expressed as acid equivalents (a.e.) of glyphosate for comparison to the literature. The concentrations used in the exposures of embryos to the formulated product were large, 9-, 11-, and 15-fold greater than the median, lethal concentrations (LC50s) (7,900 μg a.e./L) for embryos of the same species reported from the literature. Embryos showed a reduction in responses observed in the eggs of frogs and chickens to humans. Although the estimated concentrations in the eggs were lower than that in the study on embryos (based on volume of the egg and diffusion throughout the egg after injection), there is no information on the movement of the injected material from the site of injection, and the actual exposure in the treated area is unknown. In fact, the pronounced effects only at the site of injection suggest that the responses were to highly localized concentrations. In addition, the effects observed after the injection of glyphosate acid into the eggs of frogs could be explained simply by pH. Nowhere in the article is there any mention of adjustment of the pH of the treatment solutions or even what the pH of these solutions was. The pH of the dilutions of the formulated product were, but the pH normal physiological range significantly reduces responses in *in vitro* assays with cells from the same species of frog. It is not known what the pH of the dilutions of the formulated product were, but the pH of the commercial product is 4.9, 10

The suggestion in this article that glyphosate causes teratogenic effects in animals is not consistent with the large number of studies that have been reviewed by regulatory agencies and in the literature. 14 The NOEL and LOEL for teratogenicity in rabbits are 1,000,000 and 3,500,000 μg/kg/day, respectively. 11 The NOEL in a three-generation reproduction study in rats was >30,000 μg/kg/day. 11 Birds, no effects on reproduction were observed in mallard ducks or bobwhite quail after exposures to technical glyphosate up to 1,000,000 μg/kg diet. 11 Even when eggs of chickens were treated with a concentration of 5% formulated Roundup on days 0, 6, 12, and 18 days postlaying, there were no effects on hatching success. 15

In their discussion, the authors suggest that their observation may explain some of the reported cases of malformations in children born of mothers exposed to herbicides during pregnancy. In support of this, they quote an epidemiological study where exposures to glyphosate were not characterized or are based on anecdotal observations: “(Dr. Hugo Lucero, Universidad Nacional del Nordeste, Chaco; personal communication).”
In fact, the case-control study in Paraguay\textsuperscript{16} only enumerated self-reported association with pesticides ("agrotóxicos") in general, and it is unclear if glyphosate was even used in the region. The extrapolation of their findings in the eggs of frogs and chickens to humans are not supported by epidemiology studies in the literature,\textsuperscript{14} in general, or specifically to neural development in humans.\textsuperscript{17}

In summary, the study reported effects of glyphosate only at unrealistically high concentrations or via unrealistic routes of exposure. The data are inconsistent with the literature, are not suitable or relevant for risk assessment for humans or wildlife, and do not support the extrapolations to human health as stated in the conclusions.

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\textbf{REFERENCES}


\textsuperscript{(10)} Monsanto (2002) \textit{Material Safety Data Sheet Commercial Product}, p 8, Monsanto Canada, Winnipeg, Canada.


