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Letter to the Editor

Bayer CropScience's position on the findings of glufosinate and its metabolite

A recently published paper in Reproductive Toxicology by authors Aris and Leblanc reported the potential for maternal and fetal exposure to certain pesticides associated with genetically modified foods (PAGMF) [1]. The authors conclude among other things that both maternal and fetal exposure to the glufosinate metabolite 3-methylphosphinicopropionic acid (3-MPPA) results from the approved agricultural uses of glufosinate in Canada, as evidenced by detectable levels of 3-MPPA in serum samples obtained from pregnant women and their fetuses. The authors also suggest that given the biological and toxicological effects of this metabolite, which they state are similar to those of the parent compound, more studies are needed to better understand the potential impact of 3-MPPA on the fetus. Glufosinate residues were also reported, but only in plasma of non-pregnant women.

Bayer CropScience (BCS), as the primary registrant of the active ingredient glufosinate-ammonium, has several issues with the publication. We find a number of incorrect statements in the paper in addition to possible analytical inadequacies and implausibilities which we believe should be clarified.

To begin, BCS would like to point out that the metabolite 3-MPPA is not a significant residue in glufosinate-tolerant crops; the (−) isomer of *N*-acetylglufosinate (NAG) is the major metabolite in glufosinate-tolerant crops (1998 JMPR residue review) [2]. Of note, there is a complete regulatory toxicology dossier available for NAG which includes rat and rabbit teratology studies; there is no evidence of teratogenicity in either species (1999 JMPR toxicity review, and EU DAR) [3,4].

3-MPPA is a major residue in conventional crops, and a significant body of guideline toxicity studies is available for 3-MPPA which have been recently reviewed in the EU re-registration process according to Directive 91/414/EEC. BCS challenges the assertion that 3-MPPA has similar biological and toxicological effects to glufosinate based on this existing significant body of data which apparently was not known by the authors. 3-MPPA does not inhibit glutamine synthetase and therefore by definition cannot have similar biological properties (Koecher and Dickerhof) [5] and (ENV/JM/MONO(2002)14) [6]. In the 2002 EU Draft Assessment Report (DAR), the Rapporteur Member State concluded that there were no teratogenic effects in either the rat or rabbit teratology studies for 3-MPPA. The 2005 EFSA Scientific Report [7] stated that toxicity studies carried out on NAG and 3-MPPA indicate that these metabolites are of lower toxicity than glufosinate.

More importantly, BCS has reason to doubt the accuracy of the reported serum levels for 3-MPPA. Aris and Leblanc analyzed their samples according to the method described by Motojyuku et al. [8] who reported that a peak derived from endogenous plasma components interfered with analysis of 3-MPPA. Although Aris and Leblanc reported 3-MPPA in every sample of maternal and fetal cord blood and most samples of non-pregnant women, insufficient detail is provided in the publication to understand if and how the problem of interference was addressed. Therefore, BCS believes that the reported 3-MPPA could be due to an artifact of the analysis. Additional description and detail from the authors, including validation of the method with chromatograms and spectra, would be needed to prove that 3-MPPA was indeed found in serum.

Further examination of putative 3-MPPA concentrations in the plasma raises additional concerns. It is known that glufosinate and its metabolites are rapidly cleared from the body (EU DAR) [4]. Assuming 100% of the food consumed had 3-MPPA residues at the maximum allowable residue levels (MRL) and 5% of the residues are absorbed, the women would need to consume extreme amounts of food to achieve the reported levels. For example, one of the highest Canadian MRLs for a human consumable item is lentils (a non-GMO crop) at 6 mg/kg. Back calculating from the highest plasma concentration (417 ng/mL 3-MPPA equivalent to 494 ng/mL glufosinate) would require the women to consume more than 6 kg of lentils per day! In the same vein, apples (0.1 mg/kg MRL, also a non-GMO crop) would require consumption of more than 370 kg/day or corn grain (0.2 mg/kg, a GMO crop) would require consumption of more than 185 kg/day.

BCS also questions the reported glufosinate serum findings. Glufosinate residues were only reported in non-pregnant women. The authors attributed the absence of glufosinate in maternal and fetal cord blood to hemodilution. If one compares the mean putative 3-MPPA concentrations and considers them normative for hemodilution, the relative value for glufosinate in pregnant women should be well above the detection limit (the authors acknowledge there was no significant difference between 3-MPPA concentrations in pregnant and non-pregnant women). Even though the reported glufosinate concentrations are lower than claimed for 3-MPPA, the plasma levels are high relative to normal food consumption, as for the metabolite.

BCS believes that the data and rationales provided in this article are sufficient to question the accuracy and credibility of the authors' findings and conclusions related to glufosinate and the metabolite 3-MPPA.

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