Animal Carcinogenicity data

Regulatory authorities (US EPA, Canada PMRA, EU), scientific bodies (JMPR/WHO, WHO IPCS, WHO Water) and third party experts (Williams et al., 2000; Mink et al., 2012; Kier and Kirkland, 2013; Kier 2015; and Greim et al., 2015) around the world for decades have concluded that glyphosate is not gentoxic or carcinogenic. The only way that IARC could have come to an opinion so completely opposite was to: (1) disregard the opinions of the all the other scientists and pathologists who conducted the actual studies; (2) interpret findings differently/incorrectly, and; (3) rely on non-standard studies with adverse effects where the methods have not being validated, not conducted according to international guidelines, and not relevant for humans based on exposure conditions. Clearly they did not conduct a weight-of evidence evaluation or follow standard toxicological practice and evaluation frameworks that are the foundation of hazard and risk assessment (Adami et al., 2011 and Lewis et al., 2002).

Due to the lack of effective legal and regulatory provisions for the sharing of company owned study data in the past, and to guarantee the safety of technical glyphosate obtained from different processes of synthesis, several manufacturers of glyphosate had to initiate toxicological testing programs of their own. Occasionally, regulatory studies had to be repeated to reflect major changes in the underlying government regulatory test guidelines.

In the case of glyphosate, this has given rise to a multitude of studies for the same toxicological endpoints, leading to the availability of an extraordinarily robust scientific study database that can be considered unique among pesticides, industrial chemicals, and pharmaceuticals. Such a remarkable volume of studies addressing the same endpoints, conducted over the last 40 years by several independent companies and laboratories while toxicology test guidelines have evolved, provides a unique opportunity to evaluate potential human health hazards of glyphosate.

Greim et al., 2015 evaluated **fourteen carcinogenicity studies (nine rat and five mouse)**. They concluded there was **no evidence of a carcinogenic effect related to glyphosate treatment**. The authors further stated that the lack of a plausible mechanism, along with published epidemiology studies, which fail to demonstrate clear, statistically significant, unbiased and non-confounded associations between glyphosate and cancer of any single etiology, and a compelling weight of evidence, support the conclusion that **glyphosate does not present concern with respect to carcinogenic potential in humans.**

These fourteen studies were also just recently evaluated by the Germany Federal Institute for Risk Assessment (BfR) for the European Commission on the Annex 1 renewal on glyphosate. The BfR concluded that glyphosate is unlikely to pose a carcinogenic risk to humans.

It is unclear on what basis this subgroup at IARC came to the conclusion of sufficient evidence in animals. While IARC has not provided specific references for the studies they mention in the summary, it can be deduced based on our knowledge of the database and history of previous regulatory evaluations.

Kidney tumors in male mice:

- The US EPA (1993) and others since (JMPR/WHO 1986; IPCS/WHO 1994; JMPR/WHO 2004; EU 2002 and 2015; PMRA 1991; Williams et al., 2000; and Greim et al, 2015) have long determined that the renal tubule tumors found in male mice in one study (Knezevich and Hogan 1983) were not related to treatment. The leading kidney pathologist in the country and other members of a pathology working group, as well as a group of biometricians and the EPA scientists, reached the same conclusion as the study pathologist; during these reviews, it was noted that these tumors were not significantly elevated, were within the historical control range, were not seen in females, and no preneoplastic lesions were observed. Therefore, it was concluded that the tumors were spontaneous and not related to treatment and glyphosate was not considered to be carcinogenic in the study. Furthermore there are four more studies in mice with glyphosate and this tumor type has not been observed in any of them, further suggesting that kidney tumors were unrelated to glyphosate.

Pancreatic tumors in male rats

- The US EPA (1993) and others since (JMPR/WHO 1986; IPCS/WHO 1994; JMPR/WHO 2004; EU 2002 and 2015; PMRA 1991; Williams et al., 2000; and Greim et al, 2015) have long determined that the pancreatic islet cell adenomas found in male rats are not related to treatment. In one study (Stout and Ruecker 1990) there was a slightly increased incidence of pancreatic islet cell adenomas in the low-dose and high-dose males; there was no significant positive dose-related trend in their occurrence; there was no progression to carcinomas; and the incidence of pancreatic hyperplasia (non-neoplastic lesion) was not dose-related; it was concluded that these were not treatment related. The JMPR/WHO 2004 concluded "administration of glyphosate to Sprague-Dawley rats for 24 months produced no signs of carcinogenic potential."
- The other study IARC appears to be referring to regarding pancreatic islet cell adenomas is Lankas (1981). The incidence for this tumor is 0/50 control, 5/49 low dose, 2/50 mid dose and 2/50 high dose. Because of the remarkable lack of a dose response, these findings are not considered by any Regulatory agency to be treatment related.
- As there are a number of additional rat carcinogenicity studies and that this is a common tumor in rats, Greim et al, 2015 combined data from all the studies with doses ranging from 3-1290 mg/kg/day and found no dose-response.
- This is a common tumor in rats that occurs with a variable incidence, results are not consistent between studies, there is no dose-response, and the incidences were within the normal historical control range.

Haemangiosarcomas in mice

- The JMPR/WHO (2004) was the only group to discuss the haemangiosarcomas seen in mice in one study (Atkinson, 1993); they did not consider them to be caused by administration of glyphosate due to the lack of a dose–response relationship, the lack of statistical significance, and the fact that the incidences recorded in this study fell within the historical ranges for controls. Their conclusion

was "administration of glyphosate to CD-1 mice for 104 weeks produced no signs of carcinogenic potential at any dose. The NOAEL was 1000 mg/kg bw per day, [which was] the highest dose tested."

New References

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Lewis RW, Billington R, DeBryune E, Gamer A, Lang B and Carpaninin F. Recognition of Adverse and Nonadverse Effects in Toxicity Studies TOXICOLOGIC PATHOLOGY, vol 30, no 1, pp 66–74, 2002

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