



ADVERSE EFFECTS OF GLYPHOSATE AND ROUNDUP ADMINISTERED AT HUMAN EQUIVALENT DOSES TO SPRAQUE-DAWLEY RATS

Introduction

Glyphosate is a broad-spectrum, post emergent, non-selective, systemic herbicide, which effectively kill or suppresses all plant types. It has agricultural and non-agricultural uses throughout the world. It was registered in over 130 countries as of 2010 and is probably the most heavily used herbicide in the world, with annual global production volume estimate at approximately 600,000 tons in 2008 rising to 720,000 tons in 2012. The International Agency for Research on Cancer (IARC) classified glyphosate as a probably carcinogen to humans (Group 2A), but according to the EFSA (European Food Safety Authority) the evidence is not yet sufficient to declare its carcinogenicity with certainty (1). Given this state of scientific wavering, it is essential to fully understand the potential harmful effects from this substance, including other non-cancer toxicological endpoints.

Aim

This study examines whether low-dose exposure to Glyphosate and/or its commercial formulation Roundup, could be related to health effects in Sprague-Dawley rats, when the exposure starts from gestation through adulthood. The dose selected are comparable to those currently admitted in humans in the USA in order to mimic the real life exposure and the end-points studied are related to developmental, reproductive and toxicology too.

Methods

Route of administration: test substances are administered ad libitum, via drinking water

Compound tested: GLYPHOSATE and its formulation ROUNDUP®.

Study design and endpoints explored in the study are summarized in table 1 and table 2.

Table 1. Glyphosate pilot study: endpoints evaluated

GROUP	COMPOUND	DOSE
I	Drinking water	Control
II	Glyphosate	USA ADI (1.75 mg/kg/day)
III	Roundup	USA ADI (1.75 mg/kg/day)

Table 2. Glyphosate pilot study: endpoints evaluated

Group		Body weight	Water and feed cons.	Urinalysis	Clinical chemistry	Haematological tests	Organ weight	Histopathology	Micronuclei	Transcriptome	Microbiome	Litter size	Live birth index	Sex ratio	Intra/extra uterine death	Anogenital distance	Balano-preputial sep.	Vaginal opening	First estrous	Estrous cyclicity	Hormone analyses	Sperm analyses	Sperm aneuploidy	
		F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0	F1	F0
I (control)	F0	✓	✓				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	F1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
II (Glyphosate)	F0	✓	✓				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	F1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
III (Roundup)	F0	✓	✓				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	F1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Results

Glyphosate and AMPA detection: increased glyphosate excretion in urine in relation to the duration of the treatment (bioaccumulation)

Dams: increased kidney lesions

Offspring clinical chemistry: decreased total protein levels, hyperphosphatemia and BUN decrease in blood

Offspring histopathology: general increased number of animals bearing lesions in kidney, and in the hematopoietic component of liver and intestine

Offspring Micronuclei: increased in Roundup treated group

Hormones: main differences in Roundup treated group

Liver Transcriptome: main differences in female Roundup

Ano-genital Distance (AGD): increased AGD in both male and female pups treated with Roundup and in male treated with Glyphosate

First estrous: delayed first estrous observed in females treated with Roundup

Microbiome: significant and distinctive changes in overall bacterial composition in F1 pups, specifically at pre-pubertal age (PND 31).

Discussion

- The dose tested was the USA Glyphosate acceptable daily intake (ADI) which is considered to be a safe threshold.
- Our pilot study provides evidence of endocrine disturbances and potential adverse effects on rats, particularly when exposed to Roundup.
- An integrated long-term experimental project is needed to explore this early findings (2).

References

- Portier, Christopher J., et al. "Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)." J Epidemiol Community Health (2016): jech-2015.
- Manservigi Fabiana, Clara Babot Marquillas, Annalisa Buscaroli, James Huff, Michelina Lauriola, Daniele Mandrioli, Marco Manservigi, Simona Panzacchi, Ellen K. Silbergeld, and Fiorella Belpoggi. "An integrated experimental design for the assessment of multiple toxicological end points in rat bioassays." Environ Health Perspect. 2017 Mar;125(3):289-295