ADVERSE EFFECTS OF GLYPHOSATE AND ROUNDUP ADMINISTERED AT HUMAN EQUIVALENT DOES TO SPRAGUE-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 it’s formulation ROUNDUP®.
Study design and endpoints explored in the study are summarized in table 1 and table 2.

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 Trascriptome: 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

Table 1. Glyphosate pilot study: endpoints evaluated

<table>
<thead>
<tr>
<th>GROUP</th>
<th>COMPOUND</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Drinking water</td>
<td>Control</td>
</tr>
<tr>
<td>II</td>
<td>Glyphosate</td>
<td>USA ADI (1.75 mg/kg/day)</td>
</tr>
<tr>
<td>III</td>
<td>Roundup</td>
<td>USA ADI (1.75 mg/kg/day)</td>
</tr>
</tbody>
</table>

Table 2. Glyphosate pilot study: endpoints evaluated

<table>
<thead>
<tr>
<th>Group</th>
<th>Body weight</th>
<th>Water and food intake</th>
<th>Urinary chemistry</th>
<th>Clinical chemistry</th>
<th>Hematology</th>
<th>Transcriptome</th>
<th>Liver rate</th>
<th>Live birth index</th>
<th>Sex ratio</th>
<th>Immune system</th>
<th>Testes stability</th>
<th>Testes morphology</th>
<th>Ano-genital Distance</th>
<th>Microbiome</th>
<th>Bacterial counts</th>
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