

## Literature review on biological effects of Roundup herbicide and evaluation of materials safety data sheet and use instructions for Aquamaster.

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### Introduction

There is abundant evidence in the literature that I cite below that Roundup with its "active" ingredient, glyphosate, and its "inert" or "other" ingredients, such as nonionic solvents and surfactants can cause substantial biological and ecological harm to wildlife, humans and the environment. The materials safety data sheet for Aquamaster cleverly omits any reference to any materials except the active ingredient and water. Users are advised to use their own nonionic solvents and to mix Aquamaster freely with a host of other herbicides that have their own nonionic solvents and surfactants that have never been tested for biological activity in combination. Because of the exclusion of surfactants and nonionic solvents on the MSDS of Aquamaster, the user must use his/her own choice of 'other' ingredients to add to the pesticide mixture to obtain desired biological activity. The manufacturer of Aquamaster thus has been able to evade US EPA regulations that govern SARA Title III Rules regarding hazard status under section 15, Regulatory Information.

### Literature review

In June 1991, EPA classified glyphosate as a Group E carcinogen—evidence of non-carcinogenicity for humans—based on the lack of convincing evidence of carcinogenicity in adequate studies. Since this decision, a 1999 study found that people exposed to glyphosate are 2.7 times more likely to contract non-Hodgkin Lymphoma (NHL)<sup>1</sup>. In 2002, study of Swedish men showed that glyphosate exposure was *significantly* associated with an increased risk of NHL, and hairy cell leukemia—a rare subtype of NHL.<sup>2</sup> Further, a 2003 review of studies conducted on farmers by researchers at the National Cancer Institute showed that exposure to glyphosate was associated with an increased incidence of NHL.<sup>3</sup> According to the American Cancer Society, non-Hodgkin lymphoma is a cancer that starts in cells called lymphocytes, which are part of the body's immune system.<sup>4</sup>

Researchers evaluated associations between glyphosate exposure and cancer incidence in the Agricultural Health Study (AHS)<sup>5</sup>, a cohort study of 57,311 licensed pesticide applicators and found that glyphosate had a suggested association with multiple myeloma, a cancer that starts in plasma cells, a type of white blood cell.<sup>6</sup> This association with multiple myeloma was observed with use of glyphosate and cumulative exposure days of use (a combination of duration and frequency).

There is also evidence of increased birth defects, season of conception and sexual development due to one of the manufacturer recommended herbicides, 2,4-D, that can be mixed with Aquamaster,<sup>7</sup> increased risks of late abortion,<sup>8</sup> and endocrine disruption<sup>9</sup> with glyphosate use.

An increasing number of studies have found that formulated glyphosate products are more toxic than the active ingredient glyphosate alone. One study by Walsh, et al.<sup>9</sup> found that Roundup decreased steroidogenesis, indicating that at least one other component of the formulation is required to disrupt steroidogenesis since it was observed that glyphosate alone did not alter steroid production.<sup>9</sup> In 1998, researchers found that Roundup was able to induce a dose-dependent formation of DNA adducts in the kidneys and liver of mice.<sup>10</sup> The researchers concluded that the Roundup-related DNA adducts were not related to the active ingredient (the isopropylammonium salt of glyphosate) but to another, “unknown” component of the herbicide formulation. Dallegrove et al. (2003 & 2007), in studies with Wistar rats, also found that Roundup induces developmental retardation of the fetal skeleton, a decrease in sperm number, an increase in the percentage of abnormal sperms and a dose-related decrease in the serum testosterone level at puberty.<sup>11</sup> A 2004 study examining glyphosate effects on cell cycle regulation concluded that glyphosate-based pesticides are clearly of human health concern based on results that demonstrated a molecular link between glyphosate-based products and cell cycle dysregulation—a hallmark of tumor cells and human cancers.<sup>12</sup>

A 2008 study confirmed that the adjuvants in Roundup formulations kill human cells, particularly embryonic, placental and umbilical cord cells, even at very low concentrations.<sup>13</sup> These researchers found that Roundup formulations cause total cell death within 24 hrs, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase measuring membrane damage. Polyethoxylated tallowamine or POEA—a surfactant used in herbicidal products, especially Roundup—was found to be the most potent “inert” and was responsible for the elevated toxic effects.

POEA accounted for more than 86% of Roundup toxicity on microalgae and crustaceans in a study conducted by Tsui and Chu.<sup>14</sup> This study also found that an increase in pH (6-9) and increase of suspended sediment concentration (0-200 mg/l) significantly increased the toxicity of Roundup to *Ceriodaphnia dubia*. Interestingly, this study determined that the order of toxicity to aquatic invertebrates were as follows; POEA>Roundup>glyphosate acid>IPA salt of glyphosate.

Another study found that the cytotoxicity of Roundup formulations were amplified with time and that exposure affects human reproduction and fetal development.<sup>15</sup> Roundup reduces human placental JEG3 cell viability at least two times more efficiently than glyphosate, disrupts aromatase activity, and mRNA levels.<sup>16</sup> Richard, et al. in the same paper also report that glyphosate is toxic on human placental JEG3 cells within 18 hrs with concentrations lower than those used in agriculture. This effect was found to increase with concentration and time, or in the presence of Roundup adjuvants. Arbuckle, et al. found that preconception exposures to glyphosate moderately increased the risk for spontaneous abortions in mothers exposed to glyphosate products<sup>17</sup>.

EPA acknowledges that glyphosate has the potential to contaminate surface water because it does not readily break down in water or sunlight. Due to glyphosate’s potential for contamination, the agency has established a maximum contaminant level (MCL) for glyphosate (0.7ppm).<sup>18</sup> The agency lists the short- and long-term health effects for drinking

water exposures: for relatively short periods of time, congestion of the lungs and increased breathing rate; for lifetime exposure at levels above the MCL kidney damage and reproductive effects.

Glyphosate has registered use for control of emergent aquatic weeds in ditches, wetlands, and margins of water bodies. However, glyphosate and its formulated end-use products have been proven to be toxic to aquatic organisms. Glyphosate was measured at high concentrations (highest-328 µg/l) in vernal pools and adjacent flowing waters in Washington, D.C.—a concentration that exceeds the freshwater aquatic life standard for glyphosate—in a 2008 study conducted by researchers at the USGS.<sup>19</sup> A study by Relyea in 2005 found that Roundup alone is “extremely lethal” to amphibians in concentrations found in the environment.<sup>20</sup> Another study found that *Rana pipiens* tadpoles chronically exposed to environmentally-relevant concentrations of glyphosate formulations, containing POEA, exhibited decreased snout-vent length at metamorphosis, increased time to metamorphosis, tail damage, and gonadal abnormalities. These effects were due in part to disruption of hormone signaling, because thyroid hormone receptor beta mRNA transcript levels were elevated by exposure to formulations containing glyphosate and POEA.<sup>21</sup> The authors of this study concluded that surfactant compositions must be considered in the evaluation of toxicity of glyphosate-based herbicides. Native freshwater mussels, *Lampsilis siliquoidea*, were found to be the most sensitive aquatic organisms tested with glyphosate-based chemicals and its surfactants.<sup>22</sup>

The EPA requires the labeling of some glyphosate products “toxic to fish” as these products are applied directly to aquatic environments. The agency has not taken into consideration concentrations of glyphosate or Roundup that have already contaminated these water bodies via transport of residues adsorbed in soil particles suspended in runoff water, leaching and drift, phenomena it is well aware occurs.<sup>23</sup> Other environmental factors such as high sedimentation, increases in temperature and pH levels have been shown to increase the toxicity of Roundup, especially to young fish,<sup>24</sup> though they go unaddressed by the agency. The agency has already determined that glyphosate and its salts, as well as its metabolite AMPA, are likely to adversely impact the endangered California red-legged frog based on prey and habitat reduction.<sup>23</sup>

Besides all of the undesirable impacts of Roundup on aquatic invertebrates, fish, amphibians and other vertebrates including humans, the use of Roundup is also undesirable because of its potential for developing Roundup resistant weeds, which has been amply documented.<sup>25,26,7,28,29,30,31,32</sup>

Finally, there are environmentally benign alternative methods of dealing with weeds, including the spraying of mild acids such as stock solutions of vinegar which disrupt the waxy surface of leaves thereby desiccating plants and causing them to die.

## Summary

The surveyed peer-reviewed literature documents a host of problems associated with the use of Roundup including but not limited to effects on reproduction, embryonic development, endocrine, immune and neurological function as well as cancer risks. Many of these

fundamental biological processes are not part of the EPA registration process. Moreover, the registration process only addresses the active ingredient and not the other ingredients, i.e. nonionic solvents and surfactants, which can have as much or more biological impact. Some of those other ingredients, such as POEA, have been banned from countries like Australia because of their major impact on amphibian populations. The instructions to users of Aquamaster to choose their own nonionic solvents mean that compounds like POEA can be used with impunity with no repercussions to the manufacturer in terms of regulatory requirements or legal liability. The recommendations for use to users that many other herbicides can also be mixed with Aquamaster is also irresponsible since there have been no tests for any mixtures effects for the EPA biological effects categories. In the few cases where mixtures have been studied<sup>20,33,34,35</sup>, it is evident that there are significant added biological effects which again are not part of the registration process.

Finally, the EPA registration process assumes a linear dose response, which misses the nonlinear responses of biological organisms at very low doses. A study by Welshons et al. demonstrated that the EPA review process, which is based on a linear dose response assumption, can *underestimate* biological effects at low doses by up to 10,000 times<sup>36</sup>. Moreover, because of the nonlinear responses that occur only at very low doses, the greatest effects can be at the lowest doses, as was demonstrated for a common lawn chemical mixture that induced abortions and resorptions of fetuses in the very low parts per billion<sup>37</sup>.

It is also useful to note that the normal concentration range of the human hormone estrogen (estradiol) is between approximately <50 -200 pg/ml or approximately <50 – 200 parts per trillion over the normal monthly human menstrual cycle.<sup>38</sup> That range of concentration change is sufficient to inhibit (at the low concentration) release of LH and FSH from the pituitary or induce a flush of lutenizing hormone (LH) and follicle stimulating hormone (FSH) at the high end of the normal concentration range of estradiol.

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