Glyphosate, Pathways to Modern Diseases II: Celiac Sprue and Gluten Intolerance

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nhrighttoknowgmo.org/BreakingNews/Glyphosate_II_Samsel-Seneff.pdf

General Comments:

A new review by Samsel and Seneff attempts to link the use of glyphosate as a drying or ripening agent to the increased prevalence of celiac disease. In an attempt to establish causation the authors cite their own study that appeared in the journal *Entropy* in 2013 (which has been soundly refuted, see Additional Information) and several "cherry picked" publications falsely attributing hazardous health impacts with the ingestion of crops containing glyphosate. In doing so, Samsel and Seneff completely ignore the numerous studies in referred journals supporting glyphosate safety.

It is well established that glyphosate has a very low degree of mammalian toxicity as it targets a metabolic pathway which is present in plants, but does not occur in animals. Comprehensive toxicological studies in animals have demonstrated that glyphosate does not cause cancer, birth defects, mutagenic effects, nervous system effects or reproductive problems (U.S. EPA, 1993; Williams et al., 2000; Williams et al., 2012; Kier and Kirkland, 2013); European Commission, 2002; JMPR/WHO, 2004). In fact, after a thorough review of all toxicology data available, the U.S. EPA concluded that glyphosate should be classified in Category E ("Evidence of Non-carcinogenicity in Humans"), the most favorable category possible (U.S. EPA, 1993).

Similarly to the *Entropy* paper, the current review attempts to outline possible causal connections between glyphosate and numerous diseases including celiac disease (Figure 1 in the paper). Similar hypothetical causation pathways can be spun for a wide variety of other factors in the environment. Furthermore, the authors claim completely ignores other prevailing (and more realistic) hypotheses for the rise in celiac disease including an increase in gluten ingestion in the modern diet, increased detection/diagnosis or even the "hygiene theory" that westernized society has limited exposure to the bacteria that can help to strengthen the immune system.

Like Samsel and Seneff, a similar claim was put forth by Jeffrey Smith and the Institute of Responsible Technology stating that eating GM crops somehow makes a person more susceptible to acquiring gluten sensitivity. It is worth noting that this report was soundly refuted by the Celiac Disease Foundation calling it "speculative" and stating that "[t]here has been no scientific evidence put forward for a GMO/celiac disease link that is supported by the CDF Medical Advisory Board."

Samsel and Seneff's focus on glyphosate rather than consideration of other environmental exposures appears to be arbitrary and poorly supported on legitimate scientific grounds. For example, the authors

claim that glyphosate may interfere with gut microbiota (see below), however they fail to consider that the same hypothesis pertains to a wide variety of antimicrobial agents and disinfectants. Similarly, while the ability of glyphosate to inhibit cytochrome systems is highly questionable (arguable in the case of a limited number of plant enzymes and not demonstrated in mammalian systems), humans are exposed to a myriad of cytochrome inhibitors in medications, the diet (grapefruit for example), and the environment. Therefore, the basis for claims of inhibition of CYP enzyme is tenuous and has been deemed inappropriate for characterizing risk to humans by regulatory authorities. There is a long human and ecological safety record for glyphosate that shows no indication of impact on cytochrome(s) P450 resulting in an adverse effect.

While the authors draw conclusions about the health and safety of glyphosate, there is no evidence they have formal training in biological sciences or medicine. The manuscript strings together numerous observations to create a proposed chain of causation linking glyphosate exposure to various health outcomes. Many of the individual observations made are controversial, incorrect, or poorly established. None of the disease associations are supported by available toxicology testing, experimentation, or by observations associating glyphosate exposure with these disease outcomes in human populations. In short, the authors have put forth a series of elaborate hypotheses regarding causation in the absence of observable associations. In the event that any single one of the assumptions or linkages in the overall string of hypotheses is incorrect, the entire hypothesis fails. Further, biological systems are highly complex, and their approach fails to consider alternate causation hypotheses.

On the surface, this paper appears to have a high level of scientific content and a large number of references; however the authors approach is based on weakly-supported hypothetical relationships. The paper provides no new data and is of insufficient scientific quality to provide any useful information related to the safety of glyphosate. Given that the hypothetical connections made with glyphosate can be just as readily constructed for numerous alternative causes, and given that the postulated associations have yet to be observed either in the laboratory or in human populations, the content of this paper should be regarded as no more than speculation.

Specific Comments

Throughout this paper, Samsel and Seneff fail to cite the extensive literature that shows feeding GM products to animals with no detectable health maladies. Many of the authors' claims are based on two highly flawed animal studies and *in vitro* experiments with single cell types or single bacterial populations and the implications of these studies are contradicted by extensive animal data, field studies reflecting real-world conditions, and decades of successful use of Roundup herbicide weed management around the world. Numerous public authorities conclude that glyphosate does not pose any unacceptable risk to human health. These same authorities have found *in vitro* studies to be of only very limited use for regulatory decisions, as they do not take into account the realistic exposure conditions that apply to animals and humans, nor the physiological barriers (absorption, metabolism and excretion) that limit exposure.

The literature covering the safety of GM crops supports their safe application for a variety of uses including for production of animal feeds. For example, a major literature review (Snell *et al*., 2012) assessed the health impact of diets containing GM maize, potato, soybean, rice, and/or triticale on animal health. Snell *et al*. concluded "that GM plants are nutritionally equivalent to their non-GM counterparts and can be safely used in food and feed." Recent studies where GM corn was fed to weanling pigs (Walsh *et al*., (2012) and growing and finishing pigs (Buzoianu *et al*., 2012) have demonstrated that GM corn was as safe and nutritious as the non-GM counterpart. Finally, a report by (Alison L Van Eenennaam, 2013) includes publically available data on broiler performance that includes growth, feed efficiency and post-mortem condemns. These data represent more than 100 billion animals that are fed up to 100% of the organic portion of their diets as GM feeds for their entire productive lifetime. A major conclusion of the report is that "hundreds of peer-reviewed animal feeding studies have repeatedly shown that GE plants can safely be used in feed."

Samsel and Seneff rely on a small body of literature claiming that ingestion of GM crops (mainly RR) compromises intestinal flora leading to gut dysbiosis, for which there is no evidence. This further supports the claim that ingestion of GM crops exasperates gluten sensitivities. Specifically, glyphosate can significantly reduce the population of the healthy bacterial varieties in the digestive tract and this enables the overgrowth of "dangerous" bacteria and this disruption of the gut microflora exasperates gluten sensitivity. The driver behind this claim is studies by Monika Kruger showing overgrowth of pathogenic bacterium in poultry and cattle (Shehata et al., 2013; Kruger *et al*., 2013).

The studies from the Kruger lab employ unrealistic glyphosate product concentrations in an unrealistic model; attempting to use a few isolated bacterial strains in the test tube to represent the complex microbial environment of the animal gut. Overall composition of gastrointestinal flora in animals is impacted by a wide range of factors such as feed type bacterial composition of feed, feed pH, use of antimicrobial or other therapeutic agents, bacteria in drinking water, etc. While the test system employed is not terribly relevant to the real-life environment, any findings observed must also be considered in the context of these other important influences on gut flora.

The authors do not provide data adequate to support the conclusion that glyphosate in animal feed produces clinically relevant alterations of microbial flora in poultry and livestock, nor is there clinical evidence to suggest that the widespread use of glyphosate tolerant feed components in animals has resulted in an increase in livestock disease or human illness including an increase in botulism in cattle. Bovine botulism is the result of pre-formed toxins in poorly-fermented feed or in improper feed sources (cattle grazing unintentionally on dead animal carcasses), not the result of the growth of C. Botulinum in animal gut, suggesting that the results of this publication are likely irrelevant to the occurrence of bovine botulism. Most botulism in poultry is also due to ingestion of preformed toxin.

To date, no data exist, other than what is put forth by Kruger, to support the contention that glyphosate contributes to animal or human disease as a result of alterations of bacterial flora. In fact, animal feeding studies, routinely performed in poultry and cattle, have not demonstrated an alteration in nutritional performance as a result of the feeding of glyphosate tolerant feed components, and limited

studies of high concentrations of glyphosate in sheep failed to demonstrate alterations of rumen physiology. Intestinal microbes are not static and are influenced routinely by minor dietary changes.

Finally, the two animal studies Samsel and Seneff do cite are highly flawed. The study by Carman *et al*., (2013) has been widely discredited by industry, academics, and regulatory agencies (e.g., Food Standards Australia New Zealand, FSANZ). While Carman *et al*., do not report any significant differences in health, growth, and feed efficiency, the paper claims that pigs fed GM diets demonstrate an increase in uterine weight and severe stomach inflammation. Regarding uterine weight, the absence of any historical control data made it impossible to interpret the findings in the context of natural variability. Thus any attempt to make an issue around the small increase in uterine weight was unfounded. Specifically, the author's speculation that differing uterine weights are due to diet is inaccurate. When one considers the ages of the pigs, extreme variability and presence of fluid in some, uterine size might be the result of pigs in estrus (heat).

Regarding the effects on the pigs stomachs, both pigs fed either the GM or non-GM diets had some level of inflammation. Stomach inflammation is usually due to high levels of feed intake, finely ground feed, stress or poor health. They did a stat analysis that did not include all of the data, but a proper analysis resulted in no differences. Finally, regarding health, both pigs fed the GM and non-GM diets had moderate and/or severe inflammation (52%), pneumonia (57.5% and 59.7%), and a high mortality rate (13% and 14%), suggesting that management practices and/ or health of pigs were not optimal for both groups.

The second study, Senapati *et al*., (2009), looks at the effect of glyphosate formulation (Mera-71) at unrealistic exposure concentrations and durations applied directly to fish gills; not a relevant model for studying effects on the mammalian gut. Drift or runoff exposure would be a small fraction of this exposure level and the gill damage reported is an obvious reflection of chronic exposure to a high level of surfactant.

Another argument often made is that GM crops are the trigger for the ramped up immune response affiliated with gluten sensitivities. A study by DePaolo *et al*. (2011) demonstrated a role for retinoic acid, a metabolite of vitamin A, as an adjuvant promoting inflammatory responses to fed antigen in mice. In an attempt to establish a role for GM crops as the environmental trigger to initiating gluten sensitivity, the author cite the study by Paganelli *et al*. (2010) which showed that glyphosate increased retinoic acid activity in frog embryos. The European Commission called for a review of this publication and the concluded that the study "had been performed under highly artificial conditions, extremely different from what can be expected in agricultural circumstances, and that it is hardly possible to predict adverse effect on mammals on this basis."

The experiments were performed with unrealistic exposure scenarios. Under similar exposure conditions, caffeine has been shown to cause malformations in chick embryos Kobayashi *et al*. (1995). The results with caffeine in this experimental model provides important context. Caffeine, in its natural and added forms, is found in coffee, tea, cola beverages, energy drinks, chocolate and even some medicines, but does not illicit concerns about reproductive effects. In the same way, the results of these

studies are not relevant to the human and environmental safety of glyphosate and Roundup branded herbicides. Furthermore, there are no epidemiologic studies associating glyphosate-surfactant formulation used with the occurrence of craniofacial defects or any other specific birth defects in exposed humans. Regulatory authorities and independent experts around the world agree that glyphosate does not cause adverse reproductive effects in adults or birth defects in offspring of these adults exposed to glyphosate, even at very high doses.

Extended Messages:

- Glyphosate has a very low degree of mammalian toxicity as it targets a metabolic pathway which is present in plants, but does not occur in animals.
- Glyphosate has an excellent human health and environmental profile and a long history of safe use in more than 130 countries. This has been a key factor in the acceptance of glyphosate products as among the most widely used herbicides in the world. When used according to label directions, these products present no unreasonable risk of adverse effects to human health or the environment. This is confirmed by the extensive studies as well by the first-hand experience of millions of farmers and home gardeners who have used this product.
- Many of the authors' claims are based on *in vitro* experiments with single cell types or single bacterial populations and the implications of these studies are contradicted by extensive animal data, field studies reflecting real-world conditions, and decades of successful use of Roundup herbicide weed management around the world.
- Numerous public authorities conclude that glyphosate does not pose any unacceptable risk to human health. These same authorities have found *in vitro* studies to be of only very limited use for regulatory decisions, as they do not take into account the realistic exposure conditions that apply to animals and humans, nor the physiological barriers (absorption, metabolism and excretion) that limit exposure.
- The selective citation of literature reflects bias towards claiming adverse effects.
- The basis for claims of inhibition of the cytochrome enzyme is tenuous which has been deemed inappropriate for characterizing risk to humans by regulatory authorities. There is a long safety record for glyphosate that shows no indication of impact on cytochrome(s) P450 resulting in an adverse effect.

Additional Information

Links to third party reviews of Samsel and Seneff's Entropy Publication (2013):

1. http://www.huffingtonpost.com/tamar-haspel/condemning-monsanto-with-_b_3162694.html
2. I Was Going To Write Some Words But Keith Kloor Beat Me To It
3. http://blogs.discovermagazine.com/collideascape/2013/04/26/when-media-uncritically-cover-pseudoscience/#more-11062
4. http://www.biofortified.org/community/forum/agriculture-group5/growing-methods-forum26/glyphosate-disease-and-semiotic-entropy-thread302.0/
5. http://gmopundit.blogspot.com/2013/04/all-you-ever-wanted-to-know-about.html#!/2013/04/all-you-ever-wanted-to-know-about.html
6. http://pipeline.corante.com/archives/2013/04/30/is_glyphosate_poisoning_everyone.php