

SEAPHS
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California Environmental Protection Agency
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Re: Proposed No Significant Risk Level (NSRL) for the chemical glyphosate to be adopted into regulation in Title 27, California Code of Regulations, section 25705.

Dear members California Environmental Protection Agency,

Glyphosate nitrosamine contaminants. There are no safe levels of the N-nitrosamines of glyphosate found in every glyphosate product and which are also produced in vivo.

The N-nitrosamines of secondary amines are known to be carcinogenic. The nitrosamines of glyphosate are formed on a secondary amine. I now raise the issue of the N-nitrosamines of glyphosate of which there are several, because they are carcinogens and have all been essentially ignored. It appears that Monsanto and the US EPA have hidden the N-nitrosamines of glyphosate from discussion even to the point of editing and redacting data from crucial documents concerning a number of N-nitrosamines of glyphosate. I am fortunate to have received all of the Monsanto documents on the N-nitrosamines of glyphosate from the US EPA, and I can speak directly to this issue.

The nitrosamines of glyphosate are also synthetic amino acids which may participate in biology with adverse consequences. One part per trillion of glyphosate has been demonstrated to induce the growth of breast cancer cells. One part per trillion (1 ppt) may not seem like a lot. However, in 1 ppt there are over 3 billion molecules of glyphosate participating in random collisions at the molecular level.

The US EPA set a limit of 1 ppm (1,000 ppb) of N-nitrosoglyphosate in Roundup products. Monsanto trade secret documents clearly show that nitrosamines of glyphosate increase in vivo over and above what is found in the products and you may refer to the tables in the peer-reveled paper [Glyphosate pathways to modern diseases IV: cancer and related pathologies](#) Table 13 to view some of this information. Glyphosate actually increases in concentration over that measured in the original dose solutions of 14-C experiments. This is a sobering fact that must not be taken lightly. Like the drug TAMOXIFEN, Glyphosate does not behave in a dose dependent fashion, as it is non-monotonic. Today in risk assessment we now realize that there are two types of agents that can be deleterious to human and animal biology. Those that may have a threshold for intake and exposure and those that cause harm at any level above zero as noted by Kinoshita et al (Hormesis in Carcinogenicity of Non-genotoxic Carcinogens, J Toxic Pathol 2006; **19**: 111-122).

For the sake of efficiency I have provided direct copy of relative portions of my papers which speak to the issues involving the nitrosamines of glyphosate and include them as part of this letter. The reference numbers have been left in with the text and you may access them in the published papers at ResearchGate the links of which are provided at end of this letter.

Glyphosate pathways to modern diseases IV: cancer and related pathologies

The abstract which mentions a nitrosamine of glyphosate in part reads”Glyphosate has a large number of tumorigenic effects on biological systems, including direct damage to DNA in sensitive cells, disruption of glycine homeostasis, succinate dehydrogenase inhibition, chelation of manganese, modification to more carcinogenic molecules such as N-nitrosoglyphosate and glyoxylate, disruption of fructose metabolism, etc. ...”

Please see page 128 of this paper for actual real world concentrations of N-nitrosoglyphosate found in dose solutions of glyphosate and used in 14-C radio labeled studies, as well as increasing concentrations found found in faeces and urine of test animals administered this synthetic amino acid.

“Of all of the nonbasic compounds found during analysis of excreta, AMPA followed by N-nitrosoglyphosate were most prevalent. Total N-nitrosoglyphosate levels found in the animals ranged between 0.06–0.20% of the given dose. Faecal samples contained 0.10–0.32% and urine 0.06–0.15% of N-nitrosoglyphosate. Stability studies revealed that the majority of the N-nitrosoglyphosate found in the faeces was not completely due to presence of the compound as a contaminant of glyphosate, nor was it due to animal metabolism, but rather was due to the chemical reaction of glyphosate with nitrites contained in the excreta. Glyphosate readily reacts with oxides of nitrogen (e.g., NO₂) to form the metabolite N-nitrosoglyphosate. This engenders concern because N-nitroso compounds are carcinogens. Nitrous acid occurring in sweat excreta of the skin could be problematic in the presence of glyphosate and may be responsible for the rise of some skin cancers. N-nitrosoglyphosate, the product of chemical reaction between glyphosate residues and nitrites in the colon, may in fact be a causal agent in the alarming increase in colorectal cancer. We discuss N-nitrosoglyphosate in §9.

Colvin, Moran & Miller [27] evaluated the metabolism of 14C-AMPA in male Wistar rats. A 6.7 mg/kg dose of radiolabelled AMPA was administered orally, of which 20% was found unchanged in the urine of the animals and 74% in the faeces. Recovery from excreta totalled 94% of the dose. In another study, Sutherland [28] fed Sprague Dawley rats a single radiolabelled dose of N-nitrosoglyphosate and successfully quantified the metabolite in the urine and faeces. Male and female animals received 3.6 mg/kg and 4.7 mg/kg, excreting 2.8% (faeces) 88.7% (urine) and 10.7% (faeces), 80.8% (urine) respectively. **Both male and female rats retained 8.5% of the N-nitrosoglyphosate dose**, while 90.5% was eliminated in excreta.”

9. N-NITROSOGLYPHOSATE AND N-NITROSOSARCOSINE

“As was shown by Monsanto’s own studies [26], glyphosate readily reacts with nitrogen oxides to form N-nitrosoglyphosate (NNG), which is of great concern due to its toxicity [105]. N-nitroso compounds (NOCs) can induce cancer in multiple organs in at least 40 different animal species, including higher primates [106–108]. In vitro studies on human liver slices, the mechanism of action was shown to be nucleic acid alkylation [109]. Schmahl and Habs commented: “N-nitroso compounds can act carcinogenically in a large number of animal species; there is no rational reason why human beings should be an exception, all the less so since in vitro experiments have shown N-nitroso compounds are metabolized in the same way by human livers as by the livers of experimental animals” [108, p. 240]. Several different nitrosylated compounds have been targeted as potential carcinogenic agents, although it is conceded that the long lag time between exposure and tumour development makes it difficult to

recognize the links [110]. Dietary N-nitrosyl compounds especially are thought to increase the risk of colon cancer and rectal carcinoma [111, 112].

The Food and Agricultural Organization of the United Nations (FAO) has set a strict upper limit of 1 ppm NNG [113]. The accepted methodology for measuring contamination levels, proposed by Monsanto in 1986 [114], has complicated instrumentation and operation conditions and is relatively insensitive [105]. New advanced methodologies offer safer and more reliable testing methods [115, 105].

One of the pathways by which some bacteria break down glyphosate is by first using carbon-phosphorus lyase (C-P lyase) to produce sarcosine as an immediate breakdown product [89, 116]. Nitrosylated sarcosine is well recognized as a carcinogenic agent. Injection of 225 mg/kg of nitrososarcosine into mice at days 1, 4 and 7 of life led to the development of metastasizing liver carcinomas in later life in 8 out of 14 exposed animals [117].

Elevated levels of sarcosine are also linked to prostate cancer, particularly metastatic prostate cancer [118]. An unbiased metabolomic survey of prostate cancer patients identified elevated levels of serum or urinary sarcosine as a marker of aggressive disease [119] (prostate cancer is the most commonly diagnosed cancer in men in the USA, and it afflicts one in nine men over the age of 65 [120]). In both in vitro and in vivo prostate cancer models, exposure to sarcosine, but not glycine or alanine, induced invasion and intravasation [119].”

Please see paper:

[Glyphosate pathways to modern diseases VI: Prions, amyloidosis and autoimmune neurological diseases](#)

3. Glyphosate As A Glycine Analogue

“.....N-nitrosoamino acids form a reasonable model for N-nitrosoglyphosate, a carcinogenic derivative of glyphosate that was of concern to the EPA during Monsanto’s early studies. N-nitrosoproline is particularly relevant because proline, like glyphosate, has an extra carbon atom bound to the nitrogen atom. With respect to non-coding amino acids, and especially the incorporation of N-nitrosoamino acids into peptides and proteins. R.C. Massey remarked: “In addition to their presence as free N-nitrosoamino acids, species such as N-nitrosoproline (NPRO) and N-nitroso-4-hydroxyproline (HONPRO) may exist in a peptide- or protein-bound form as a result of N-nitrosation of an N-terminal imino acid residue” [62]. Tricker et al. [63] and Kubacki et al.[64] devised high performance liquid chromatography–thermal energy analyser (HPLC–TEA) techniques for analysis of multiple dipeptides with a nitrosylated N-terminal, including N-nitrosopropylalanine (NPROALA),N-nitrosopropyl-4-hydroxyproline (NPROHOPRO) and N-nitrosopropylglycine (NPROGLY) [63, 64]. Tricker notes that the average recoveries for NPROALA, NPROHOPRO and NPROGLY, 200 µg of which was added to cured meat, were between 69 and 88%. Tricker also used the method to analyse the nitroso-tripeptide N-nitrosopropylgly-cylglycine [65].

Nitrosamines of glyphosate (N-phosphonomethylgly-cine), its salts and esters include: N-nitrosoglyphosate (NNG)(Monsanto CP 76976), N-nitrosoiminodiacetic acid (NNIDA), N-nitrosoglyphosate sodium salt (NNGNa), N-nitrosoglyphosate isopropylamine ester (NNGIPA), N-nitrosoglyphosate potassium salt (NNGK), the metabolite N-nitrosoAMPA (NNAMPA), the metabolites N-nitrosodi-methyl amine (NDMA) and N-nitrososarcosine (NSAR), which occur in glyphosate products or may be generated in vivo or in soils and waterways. N-nitroso compounds derived from secondary amines are considered carcinogenic.

Monsanto glyphosate documents reveal analysis and quantification of five nitrosamines of concern [61]. Out of six lots of Roundup analyzed for NNG, four lots contained NNG residues of 0.61 to 0.78 ppm and two lots had residues from 0.22 to 0.40 ppm NNG. Analysis of six lots of Monsanto Rodeo revealed NNG residues in the range 0.13–0.49. ”

The document by Hirsch reference 61 above, also shows significant levels of other nitrosamines of glyphosate one of which was equivalent to the levels found of N-nitrosoglyphosate. Monsanto and the US EPA have suppressed these documents. I find that the hiding of these documents and this information is most disturbing. The public and scientific community deserve to know and have access to these important documents.. SEE: Hirsch, R.H., Augustin, D.J. Nitrosamine analyses of Roundup herbicide, Rodeo herbicide, MON 0139 and Polado Technical (unpublished study RD835). St Louis, Missouri: Monsanto Agricultural Company (4 November 1987).

Of the many types of cancers detailed in the Monsanto animal studies the data of which is shown in Glyphosate pathways to modern diseases IV, I draw your attention to the data on malignant lymphoma. Statistically significant data was found in the female rats of the 1981 Lankas and Hogan study and I have extracted that data and posted it to ResearchGate for convenience. A copy is included at the end of this letter. You will note that malignant lymphoma occurred in 14 different tissues. You will also note that the female control rats not fed glyphosate were not stricken by this type of malignant cancer. Only the glyphosate treated rats of this sex and groups receiving glyphosate in the diet got malignant lymphoma. Glyphosate can be seen in this light, as a causal agent of malignant lymphoma. This is not coincidence.

A thorough consideration of Glyphosate cannot be had without a deep investigation and understanding of the nitrosamines of glyphosate which are carcinogens. Make no mistake, all Roundup glyphosate-based herbicide products, as well as ingested glyphosate residues are responsible for carcinogenic N-nitrosamine compounds for which the human and animal populations are and will be exposed. Glyphosate and its nitrosamines do not belong in any biology. I ask that you set a zero tolerance for Glyphosate in food, air, water and soil.

There are no safe levels of Glyphosate.

Kind regards,

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"In the past the world suffered grievously from lack of knowledge, today it suffers from its rejection." ~ Dr. Arthur D. Little

https://www.researchgate.net/publication/283490944_Glyphosate_pathways_to_modern_diseases_IV_cancer_and_related_pathologies

https://www.researchgate.net/publication/305318376_Glyphosate_pathways_to_modern_diseases_V_Amino_acid_analogue_of_glycine_in_diverse_proteins

https://www.researchgate.net/publication/305318376_Glyphosate_pathways_to_modern_diseases_V_Amino_acid_analogue_of_glycine_in_diverse_proteins

**Malignant Lymphomas found in female rats administered glyphosate in the diet. Data extracted from Monsanto 2-year study
Lankas & Hogan (1981)**

Glyphosate Dose mg/kg/day number affected / number of animals	0 control	5 treated---->	10	30
BRAIN	0/50	0/50	0/50	1/50 (2%)
SPINE	0/50	0/50	0/50	1/50 (2%)
HEART	0/49	1/50 (2%)	0/50	1/50 (2%)
LUNG	0/49	1/50 (2%)	0/49	1/50 (2%)
LIVER	0/50	0/50	1/50 (2%)	2/50 (4%)
THYMUS	0/25	0/32	1/37 (3%)	1/34 (3%)
SPLEEN	0/50	0/50	1/50 (2%)	2/50 (4%)
STOMACH	0/50	0/50	0/50	1/50 (2%)
BONE MARROW	0/46	0/44	1/46 (2%)	1/45 (2%)
ADRENAL GLAND	0/50	0/50	0/50	1/49 (2%)
HARDERIAN GLAND	0/47	0/45	0/47	1/44 (2%)
LYMPH NODE MESENTERIC	0/42	0/39	0/48	1/47 (2%)
LYMPH NODE MANDIBULAR	0/2	0/3	0/6	1/6 (17%)
LYMPH NODE MEDIASTINAL	0/33	0/29	1/37 (3%)	2/30 (7%)

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