Glyphosate re-assessment in Europe is corrupt: Toxicology

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In January of 2014, the German rapporteur member state (RMS) submitted their draft renewal assessment report (RAR) on the re-approval of glyphosate to the European Food Safety Authority (EFSA) [1]. The RMS did not actually review the published toxicology studies themselves, but instead relied on a summary provided to them by the Glyphosate Task Force (GTF). The GTF is a consortium of chemical companies in Europe [2]. The bulk of the RAR dealing with toxicology is word-for-word from the GTF, with comments inserted by the RMS in italics. Very little of the 947-page document on toxicology is in italics.

1. The RMS has accepted, without question, virtually all of the unpublished reports given to them by the chemical companies. Much of the information is blacked out (author, report title, laboratory) but the sponsoring company is named (Monsanto, Syngenta etc.) and the reports are referred to by a number.

2. When the industry toxicology reports were in conflict with each other, they chose to sanction the ones that reported less toxic responses, relegating others to "supplementary" status.

3. Of the published reports, they only used those that tested for glyphosate alone. The glyphosate was "supplied by Monsanto at 99% purity."

4. The GTF took all of the peer-reviewed studies and proceeded to find excuses to throw out the ones that didn't agree with the already accepted industry studies. First they threw out all studies that used the actual product (Roundup, Rodeo, Lasso etc.) because the active ingredient percentage is not the same from product to product and the surfactants used vary from product to product so the results cannot be compared and are thus inconclusive. They threw out any studies where they deemed that the dosage was unreasonably high, compared to their "safe" levels, that they decided were inapplicable to mammals (frog embryos, insect larvae etc.), that were administered in a non-natural way (injection). Then they took issue with how many rats/mice/dogs/guinea pigs were or were not used and how things were or were not measured.

5. For human studies, the GTF argued that the dose/response could not be determined, the toxic effect could not be traced to glyphosate alone, the application rates were unreasonable for Europe or there were reporting deficiencies of some sort.

The nitty gritty

In typical bureaucratic fashion, the RAR report is massive and practically impenetrable. It consists of 15 documents and a total of 3,744 pages [3]. Only the parts of the RAR concerning toxicology were examined for this report: Parts of Vol. 1, Vol. 3 Annex B.6.1, and the List of information, tests and studies which are considered as relied upon by the RMS for evaluation.

Let us be clear: all studies found toxic effects for both acute (single dose), subchronic (short-term) and chronic (long-term) exposures at some dosage. The way this game is played is to vary the dose and find the maximum dose where no adverse effects are observed (NOAL). Then divide that by 100 and declare the substance "safe". Furthermore, they continue to rely on industry-sponsored studies from the 1980s and 1990s to determine these values. Does anyone know what we are now exposed to via air, water and food? How about exposure over 20 years? We are now beginning to see these effects.

The NOALs (No Observed Adverse Effect Level) and LOALs (Lowest Observed Adverse Effect Level) were taken from industry studies. From these, the Acceptable Daily Intake ADI was calculated as 1/100 of the NOAL. The lowest NOAL was 50 mg/kg bw/day for the maternal rabbit, the most sensitive. In actual fact, the lowest observed was 20 mg/kg bw/day for the maternal rabbit, reported in a Feinchemie-sponsored study (1993), but they discounted that one and relegated it to the "supplemental" category [4]. They propose a new ADI of 0.5 mg/kg bw/day, an increase from the current 0.3 mg/kg bw/day in Europe.

Only the active ingredient, glyphosate was examined in the bulk of the toxicology evaluation. Studies of an actual product containing glyphosate were considered "of limited value" for this reassessment even though, "taken as a whole, the published data suggest a higher toxicity of certain formulations as compared to glyphosate itself" [Vol. 1, p. 38]. **Presumably only pure glyphosate is actually used in Europe.**

"In many publications, the title or the conclusions are misleading because it is claimed that the active substance (a.s.) glyphosate had been tested but actually it was a specific formulation. Composition of the tested products, apart from glyphosate content, was mostly not reported. Therefore, this data is of limited value for this toxicological evaluation that is focussed [sic] on the active ingredient" [Vol. 1, p. 38].

Absorption, distribution, metabolism and excretion in mammals

Overall findings: "Following oral administration to rats, glyphosate is rapidly absorbed from the gut but only to a limited extent of approximately 20 %. The absorbed portion is widely distributed with highest concentrations occurring in bone, kidneys and liver. Its elimination via urine is fast and complete, predominantly within 48 h. There is virtually no metabolism of absorbed glyphosate in rats. Unabsorbed substance is excreted in faeces, mostly unchanged, with only a small amount transformed to aminomethylphosphonic acid (AMPA). There is no evidence of accumulation of glyphosate" [Vol. 1, p. 39].

These findings were based on six unpublished, industry-sponsored studies [5-10], three peer-reviewed studies [11-13], and one industry study that was categorized as supplemental. In addition, there were five industry studies mentioned from the previous DAR with two of those being relegated to supplemental status. Three additional studies, two peer-reviewed [14, 15] and one unpublished [16] were mentioned but were not included in the RAR. No reason was given, nor were these assigned a category as outlined above.

All data obtained with formulations were not assessed because they are, "Not relevant for this section dealing with toxicokinetic behaviour and metabolism of the active substance" [Vol. 3 Annex B.6.1., p. 48].

According to the RAR, "Toxicokinetics and metabolism of glyphosate were seldom subject to investigations of industry-independent researchers and, thus, experimental data in open literature is scarce" [Vol. 3 Annex B.6.1., p. 46]. One of the two studies [14], mentioned but not included in the re-assessment, reported a much higher absorption rate (35 – 40%) and a metabolite aminomethyl phosphonic acid (AMPA) in the intestines and colon. Seven days after application, the total body burden was approximately 1% of the administered dose and was primarily associated with the bone. "The authors reported AMPA to be a product of metabolic activity of intestinal microbes" [Vol. 3 Annex B.6.1., p. 46].

From one of the published studies that was included [13], “After oral administration, glyphosate was partially and slowly absorbed with a T_{max} of 5.16 h. The oral bioavailability of glyphosate was found to be 23.21%. Glyphosate was converted to AMPA. The metabolite AMPA represented 6.49% of the parent drug plasma concentrations. The maximum plasma concentrations of glyphosate and AMPA were 4.62 and 0.416 µml-1, respectively. The maximum plasma concentration of AMPA was achieved at 2.42 h. For AMPA, the elimination half-life ($T_{1/2}$) was 15.08 h after oral administration of glyphosate parent compound” [Vol. 3 Annex B.6.1., pp. 46 & 47].

The unpublished study that was not included was the test results of glyphosate residues in urine samples in Europeans by Friends of the Earth [16]. This study clearly showed not only glyphosate residues, but also AMPA residues. The glyphosate residues were attributed to food, but the authors of the RAR insist that the AMPA must be from some other source because, “virtually no metabolism of glyphosate to AMPA may be expected” [Vol. 3 Annex B.6.1., p. 48]. Did different people write these paragraphs? Isn't the glyphosate metabolized by the intestinal microbes as reported in [13] above?

Since this report was prepared, a paper has been published by Kruger et al. [17] showing approximately equal amounts of glyphosate residues in the urine, kidney, liver, lungs, spleen, muscles and intestines of dairy cows. It seems that this shows that glypohsate does accumulate in the body.

Acute toxicity

A total of of 145 unpublished, industry-sponsored acute studies were submitted, most from the previous DAR. From these they deduced that there is no acute oral toxicity at the recommended levels.

At higher single doses, the following symptoms were observed: lung congestion, male heart weight reduced, ruffled fur, subdued behaviour, hunched appearance, lethargy, lack of muscle coordination, difficulty breathing, weight loss, abnormal gait and/or limb position, diarrhea, excess urine, salivation, reduced fecal volume, urinary incontinence, hair loss on the abdomen, convulsions, muscle tremors, red nasal discharge, clear oral discharge, urinary & fecal staining of the abdomen, enlarged spleen, enlarged liver, blood spots in the kidney, GI tract of dead rats with dark/red fluid.

There were no published studies on acute toxicity.

Eye and skin irritation

There were 13 unpublished, industry-sponsored acute (single application) skin studies on rats, 12 on rabbits, 11 on guinea pigs and 1 mouse study. There were 3 longer (>20 days) unpublished, industry-sponsored skin studies, 1 on rats, 2 on rabbits. All unpublished, industry sponsored studies. From these they deduced that there are no effects on skin at occupational exposures.

There were 13 unpublished, industry-sponsored studies on eye irritation. From these they deduced that there is severe eye irritation and a recommendation was made to state that on the label. This is the **only** toxic effect that they are admitting.

There were no peer-reviewed studies on eye or skin irritation.

Subchronic toxicity (90-day feeding)

A total of eight 90-day studies in rats were used for the evaluation of which 5 had been evaluated in the previous DAR. There were two 90-day studies in mice. There were four 90-day studies and four 1-year studies in dogs. All were unpublished, industry sponsored studies. The conclusion was that glyphosate is non-toxic at the recommended ADI. Brief mention was made of two published studies, one on rats and one on mice by the same authors. Neither were listed as having been used in this reassessment.

At higher doses, the following symptoms were observed: heart weight reduced in males, diarrhea,

dehydration, fur loss, reduction in body weight gain, enlarged liver and kidneys, enlarged and fluid-filled caecums (in the large intestine-indicates digestion problem), gaseous distension of the stomach, atrophy of the intestines characterised by flattening of the intestinal mucosa, inflammation in the liver, oesophagus and lungs, pneumonia, and one uterine tumor that was considered unrelated to glyphosate. Significant blood chemistry alterations included: low hemoglobin (anemia), decrease in calcuim, increase in alkaline phosphatase (associated with liver disease and hyperparathyroidism) activity, decrease in albumin (the body's predominant serum-binding protein; low albumin is associated with malnutrition, kidney, liver or intestinal problems or cancer), increased creatine phosphokinase (thyroid, heart or brain problem), increased inorganic phosphorus (possible problems with kidney or thyroid), decrease in glutamic pyrvic transaminase (liver problem) and an increase in blood urea nitrogen (kidney problem), hepatitis (males), papillary necrosis in the kidney (males), mineral deposition in kidneys.

Genotoxicity

Ten unpublished, industry-sponsored *in vitro* studies were evaluated, along with four more relegated to supplemental status. All were negative with respect to mutagenicity. Nine unpublished, industry-sponsored *in vivo* studies were evaluated. Eight were negative and one was "weakly positive" at the highest dose. "In contrast to studies with the active ingredient that were, with one possible exception, negative, findings obtained with formulations were contradictory." For this reason they assessed studies with formulations in this section. "A total of eight mutagenicity studies using four different glyphosate formulations was made available to the Rapporteur by the companies Monsanto and Cheminova. ... The studies are reliable since they were performed at least to a large extent in compliance with current OECD guidelines" [Vol. 3 Annex B.6.1, p. 376].

"Four glyphosate formulations were tested for mutagenicity in the reverse mutation assay in bacteria as well as in vivo by means of the mouse bone marrow micronucleus test. Unequivocally, all these products proved negative in both test systems. Thus, it can be concluded that the formulations Rodeo, Roundup, Direct and Glifos containing either the IPA or the ammonium salt of glyphosate, alone or in combination with different surfactants, do not cause point (gene) mutations in various Salmonella typhimurium strains and are devoid of a clastogenic potential in vivo" [Vol. 3 Annex B.6.1, p. 379].

Eight studies published in the 1990s confirming genotoxicity and mutations were considered unacceptable:

Rank et al. [18] was Not Reliable because, ".. test does not comply with current guideline requirements, ... The data obtained are so controversial that a reliable interpretation is not possible." [Vol. 3 Annex B.6.1, p. 385]

Bolognesi et al. [19] was Not Reliable because, "The outcome of the micronucleus test with glyphosate a.i. is at least surprising since much higher doses of this compound had been tested before and did not reveal indications of clastogenicity .. .the number of animals used was too low since a group size of at least five is recommended. A dose response cannot be assessed since only one dose level was included. The basis for statistical comparison is questionable since it is not clear when the six control animals were sacrificed because only one group mean value was indicated. Due to these deficiencies, this isolated positive finding is not considered to provide sufficient evidence to contravene the previously obtained negative results regarding the active substance" [Vol. 3 Annex B.6.1, p. 386].

Two papers by Lioi et al. [20, 21] finding chromosome aberrations were Not Reliable because, "The results are questionable because a number of well performed and validated studies in vitro in mammalian cells and in vivo in mammals did not register comparable effects even in dose levels more than 10 times higher than the doses used in the studies described ... replication would be needed to confirm such aberrant results" [Vol. 3 Annex B.6.1, p. 387].

Clements et al. [22] observed DNA damage but was considered Not Reliable because "... it appears equivocal whether the observed impact on the DNA was indicative of a true mutagenic effect or rather caused by cytotoxicity. ... At this time, it is not clear whether a positive result of this test obtained in tadpole erythrocytes, even if it was actually due to mutagenicity, would be of any relevance to human beings exposed. In particular, this is doubtful when the strong body of evidence that neither glyphosate nor its formulations are mutagenic as coming from many studies in various test systems is taken into consideration. .... Again, the application of results obtained with one formulation to others must be critically regarded" [Vol. 3 Annex B.6.1, p. 388]. [much of their studies were done on bacteria]

Peluso et al. [23] also observed DNA damage but was considered Not Reliable because, "Biological significance of the results is equivocal. ... It is known that DNA adducts may be formed not only as a result of direct interaction of cellular DNA with chemicals but also occur naturally or can be even related to a treatment-dependent increase in endogenous metabolites. Thus, further characterisation of these adducts and clarification of their nature would be desirable" [Vol. 3 Annex B.6.1, p. 389].

Kale et al. [24] found a positive result for mutations but was Not Reliable because, "This test system is not considered predictive for mutagenicity in mammals [test was on Drosophilia melanogaster larvae (fruit fly)]" [Vol. 3 Annex B.6.1, p. 389]. [much of their studies were done on bacteria]

Vigfusson et al. [25] found mutations in human cells but was Not Reliable because, "Test material was a formulated product containing surfactant. Only very minor changes in SCE were reported, with a limited data set of two donors and a lack of dose-response. Statistical analysis was not feasible with this very limited data set" [Vol. 3 Annex B.6.1, p. 438]

Overall assessment: "In the whole, the published data are not sufficient to provide convincing evidence of mutagenic effects caused by glyphosate or its formulations" [Vol. 3 Annex B.6.1, p. 390].

In vivo studies: Nine valid, unpublished, industry-sponsored *in vivo* studies "confirmed" no genotoxicity.

As reviewed by Williams et al. [26] 15 studies examined: 13 negative; 2 positive. Two more added since 2000 that were inconclusive for a total of 17 publications considered acceptable: 13 negative; 2 positive; 2 inconclusive. It seems they are completely relying on this review by Williams, rather than examining the studies themselves.

"Exceptions were mostly observed in unusual test systems but there are also some unexplained discordant positive results in more widely used mammalian systems. However, these occasional findings are by far outweighed by the negative high quality studies reported above. Likewise, several reports of positive results for DNA damage endpoint by means of the SCE (sister chromatid exchange), the alkaline SCGE (single cell gel electrophoresis) and the comet assay have been published for glyphosate and certain formulations. The data suggest that these effects were likely due to cytotoxic effects (e.g., of surfactants) at high concentrations rather than to DNA reactivity.

Taking a weight of evidence approach, it may be concluded that there is no i*n vivo* genotoxicity and mutagenicity potential of glyphosate or its formulations to be expected under normal exposure scenarios, i.e., below toxic dose levels." [Vol 1. p. 61].

Nine more recently (since 2000) published studies reporting positive results were deemed unacceptable.

Alvarez-Moya et al. [27] reported genotoxic activity but was Not Reliable because, "Exposure conditions of plants (immersion) not representative for glyphosate. Inappropriate test model as herbicides are toxic to plants. Presentation of results not sufficient for assessment" [Vol. 3 Annex B.6.1, p. 424]

Bolognesi et al. [28] reported possible genotoxicity from occupational exposure but was Not Reliable because, “Exposures to multiple pesticides with no information on exposure concentrations to individual pesticides make result unreliable for glyphosate” [Vol. 3 Annex B.6.1, p. 426].

Cavas et al. [29] reported abnormalities and DNA strand breaks but was Not Reliable because of, “Methodological and reporting deficiencies” [Vol. 3 Annex B.6.1, p. 428].

Guilherme et al. [30] reported positive genotoxic indicators positive but was Not Reliable because, “No positive controls were included, which significantly detracts from the utility of a non-validated, non-standard test method” [Vol. 3 Annex B.6.1, p. 429].

Manas et al. [31] reported that AMPA was genotoxic in the three performed tests but was Not Reliable because of, “Reporting deficiencies” [Vol. 3 Annex B.6.1, p. 431].

Manas et al. [32] reported an increase enzyme activities indicating genotoxicity but was Not Reliable because of “Reporting deficiencies” [Vol. 3 Annex B.6.1, p. 431].

Mladinic et al. [33] found that glyphosate does not pose a health risk and was deemed Reliable With Restrictions: Non-GLP, non-guideline in vitro study, meeting scientific principles [Vol. 3 Annex B.6.1, p. 432].

Mladinic et al. [34] reported potential DNA harm but was found Not Reliable because, “Non-GLP. Not relevant (Proposed mechanism of genotoxicity (invitro) is not relevant to human exposure levels” [Vol. 3 Annex B.6.1, p. 433].

Paz-Y-Mino et al. [35] reported that aerial spraying glyphosate had a genotoxic effect on the exposed individuals in Equador but was found Not Reliable because “Documentation of Comet assay insufficient for assessment... Not relevant (Glyphosate formulation was applied at much higher dose rates than recommended for the intended uses in the EU” [Vol. 3 Annex B.6.1, p. 434].

Poletta et al. [36] reported DNA damage in Caiman embryos but was Not Reliable because, “Non-GLP. Not relevant. Highly artificial in ovo exposure scenario not relevant to real world environmental exposures” [Vol. 3 Annex B.6.1, p. 435].

Studies of actual humans (farm workers etc.) received comments like: “ there is a significant question as to how long the blood samples used in the study were stored prior to initiating cultures and this may have affected the micronucleus numbers observed in the different sets of samples and populations.”

“However, the pattern of the increases did not correlate either with the application rate or with self-reported exposure.”

“causality of the observed effects could not be determined using reasonable criteria and that lack of exposure data precluded conclusions.”

“uncontrolled or inadequately characterized variables, such as uncharacteristic exposure to genotoxic pesticides, factors related to either high surfactant exposure, unusual GBF components in this formulation or other undocumented variables appear to be confounding factors.”

“Results were significantly inconsistent between two seasons. Although some suggestions of effects were reported, glyphosate was only one of a number of applied pesticides and the effects observed were considered as possibly attributable to exposure to Daconil® fungicide.”

Finally, “both positive and negative results have been reported for glyphosate and GBFs in the nine in vitro chromosome effects assays published after the Williams et al. [26] review. It is noteworthy that many of these studies have various deficiencies in conduct or reporting compared to internationally accepted guidelines for conduct of in vitro chromosome aberration or micronucleus studies.

“Perhaps the most significant deficiency was that coding and scoring of slides without knowledge of the treatment or control group was not indicated in seven of nine publications. This could be a deficiency in conducting the studies or perhaps a deficiency in describing methodology in the publications. Other common deficiencies included failure to indicate control of exposure medium pH, no use of exogenous metabolic activation and no reporting of concurrent measures of toxicity.”

“The conclusion of this analysis was that glyphosate and Roundup GBFs were not mutagenic or genotoxic as a consequence of direct chemical reaction with DNA. This was supported by a strong preponderance of results indicating no effects in in vivo mammalian assays for chromosome effects and consistently negative results in gene mutation assays. Although some DNA damage responses were noted, these were judged likely to be secondary to toxicity rather than DNA reactivity.” [Vol. 3 Annex B.6.1, p. 420].

Carcinogenicity

Overall finding: “The chronic toxicity/carcinogenicity part is mainly based on the extensive descriptions of the available valid studies which were provided by the GTF in its dossier. For higher efficiency of the review and for the sake of transparency, the descriptions of methods and study results in the GTF dossier were virtually not amended and even the conclusions were kept as provided. However, each study that is described in detail was commented by RMS. A paragraph on testing of formulations for long-term effects in rats has been included”[Vol. 3 Annex B.6.1, p. 439].

At high doses the following was reported: low body weight, enlarged liver , enlarged kidney, pronounced salivary gland findings (cellular alterations), stomach mucosal inflammation, cataracts, low pH in urine, adipose infiltration of bone marrow (hypoplasia), AP and ALAT activity increased, bilirubin increase, kidney papillary necrosis, prostasis and peridontal inflammation, diarrhea, tail mass increase due to abcesses, caecum distented and enlarged, dark appearance of urine, enlarged thymus, increase in mineral deposits in brain, histological findings in liver and bladder, higher incidence of malignant lymphoma, prolapse and ulceration of anus.

A total of eight new unpublished, industry-sponsored long term studies on rats and mice were accepted, and 5 (3 rat, 2 mouse) from the previous DAR that were re-evaluated and deemed acceptable.

Published studies:

“Chruscielska et al. [37] examined the chronic toxicity and carcinogenicity of glyphosate (not further specified) when administered as a 13.85 % solution of the ammonium salt at concentrations of 0, 300, 900, and 2700 mg/L in drinking water over 2 years to Wistar rats. The group size of 85 male and 85 females per concentration was quite large. There was no evidence of a carcinogenic effect and no other adverse findings were obtained that could be allocated to treatment” [Vol1. p. 68] This study was found Reliable With Restrictions (category 2). [Vol. 3 Annex B.6.1, p. 542]

“George et al., [38] used a 2-stage cancer model in mice to evaluate a glyphosate formulation for tumor promotion. A known tumor promoter, 12-o-tetradecanoyl- phorbol-13-acetate (TPA) was used as a positive control and for comparison with glyphosate effects after exposure to a tumor initiator, 7, 12-dimethylbenz[a]anthracene. Proteomics were later applied to extrapolate a basis for glyphosate formulation tumor promotion. The results are considered by the authors to indicate a tumor promoting potential of glyphosate. However, the formulation Roundup was used in the study and not the active substance glyphosate” [Vol1. p. 68] “The authors use glyphosate as a synonym for what is really a glyphosate based formulated product. Doses in this study are not representative of human exposures to glyphosate or glyphosate based formulations” [Vol. 3 Annex B.6.1, p. 539]. This study was considered Reliable With Restrictions (category 2).

Human epidemiology data

“In the following, publications suggesting that glyphosate was associated with any cancer outcome are discussed. It should not be forgotten that ”glyphosate”, in this context, in fact means glyphosate-containing herbicides that may be or may be not associated with a certain cancer type. ... An inherent weakness of many epidemiological studies is the uncertainty about exposure. Suggested associations between health outcomes and any possible causative agent are merely speculative if exposure is not known ” [Vol. 1, p. 69]

“Agricultural Health Study (AHS) which included glyphosate. Dozens of publications have resulted from data generated in this study of approximately 57,000 enrolled farmers/pesticide applicators. Blair et al.[39] provided an overview of cancer endpoints associated with different agricultural chemicals reported in earlier AHS publications. Glyphosate was not found to be associated with leukemia, melanoma, or cancers AHS data evaluating glyphosate use and multiple cancer endpoints. No association had been found for glyphosate with cancers of any type, including cancer of the lung, oral cavity, colon, rectum, pancreas, kidney, bladder, or prostate, with melanoma, all lymphohematopoietic cancers, Non-Hodgkin’s lymphoma (NHL) and leukemia, ... but a “possible association” between glyphosate use and multiple myeloma was mentioned.” [Vol. 3 Annex B.6.1, p. 522-3] The Blair publication was Reliable With Restrictions (category 2), likely because if the “possible association” with myeloma.

The following epidemiology publications [some relying on AHS data as in Blair et al.] did not find an association between glyphosate exposure and cancers of the prostrate [40-42], stomach and esophagus [43], brain [44], breast [45], in children [46], pancreas [47], Hodgkin's lymphoma [48], multiple myeloma [49], or gammopathy (abnormal blood proteins) [50]. These were all awarded with a category 1 (Reliable):

Seven published studies showing links between glyphosate and cancer were deemed not acceptable. Three studies were deemed “reliable with restrictions”, one suggested a possible association with multiple myeloma, one potential with skin tumors, one said glyphosate is not harmful.

Rejected studies:

Hardell et al. [51] reported a possible link to non-Hodgkin's Lymphoma but was Not Reliable because, “Study prone to selection and recall bias. No evidence of relevant glyphosate exposures. Not relevant (Exposure to multiple chemicals)” [Vol. 3 Annex B.6.1, p. 526].

Hardell et al. [52] again reported a possible link to non-Hodgkin's Lymphoma & hairy cell leukemia but was Not Reliable because, “No information about exposure duration, exposure concentration, as well as medical history, lifestyle factors” [Vol. 3 Annex B.6.1, p.528].

Fritschi et al. [53] reported increases in risk of non-Hodgkin's lymphoma but was found Not Reliable because, “No information about exposure duration, used glyphosate products, exposure duration and application rates. Documentation is insufficient for assessment” [Vol. 3 Annex B.6.1, p. 529].

De Roos et al. [54] reported that glyphosate is potentially carcinogenic but was Not Reliable because, “No useful information about exposure duration, exposure concentration, as well as medical history, lifestyle factors” [Vol. 3 Annex B.6.1, p. 530].

Eriksson et al. [55] reported a positive association between glyphosate and NHL but was Not Reliable because, “Multiple avenues for bias were introduced in study design, execution and data processing. No information about exposure duration, used glyphosate products and application rates” [Vol. 3 Annex B.6.1, p. 531].

Seralini et al. [56] reported liver congestions and necrosis, kidney nephropathies and tumors but was Not reliable because, "The study was performed to investigate the long term toxicity and carcinogenicity. However the study design does not agree with the OECD guidelines; Glyphosate formulation not glyphosate alone was tested" [Vol. 3 Annex B.6.1, p. 541] and, "[A] comprehensive critical assessment was published by EFSA (2012). The conclusion was that 'the currently available evidence does not impact on the ongoing re-evaluation of glyphosate...'. This opinion on the Séralini study is agreed with and supported by the RMS" [Vol1. p. 69].

Developmental and reproductive toxicity

"No evidence of reproductive toxicity was observed. Equivocal effects suggesting a lower litter size were only seen far above the limit dose. Weak effects on the offspring were indicated by a reduced pup weight but were confined to parentally toxic dose levels" [Vol 1. p. 72].

Four previously submitted studies and three new ones on rats were considered along with four previous studies and three new on rabbits. All were unpublished, industry-sponsored.

At higher doses: enlarged liver and kidney, low body weight in both adults and offspring, cellular changes in salivary glands (lesions), caecum distented and enlarged, low body weight in offspring, reduced sperm count, loose stool, fewer pregnancies, anomalous fetuses and greater percentage of malformations in litter, cardiac malformation (interventricular septal defect) in offspring, more spontaneous abortions, (post-implantation loss), higher mortality in dams.

"There were 18, 12, 15 and 13 viable litters at 0, 50, 150 and 450 mg/kg bw/day, respectively. The concurrent control showed low mean values for embryonic deaths and post implantation losses when **compared with historical control values**. **When compared with these historical data** as noted above, mean values in the treated groups were within the expected range; therefore, it was concluded that no adverse effect on foetal survival was attributed to glyphosate" [Vol. 3 Annex B.6.1, p. 644, emphasis added].

"Several of the cardiovascular malformations that were observed, particularly in the high-dose group, occurred in the same animals and are related to a single morphogenetic mechanism (i.e., displacement of the developing aorticopulmonary septum), which is likely to adjust during the first two weeks of postnatal life. These related findings, which often cluster together, included dilated/narrow aorta and narrow/dilated pulmonary artery; interventricular septal defect; and disproportionately sized right and left ventricles. These findings were observed (often in clusters) in the **historical control data** that were provided by the conducting laboratory." [emphasis added]

"Individual presentation of these malformations in tables when the malformations occurred together in the same foetus and are due to the same mechanisms and artificially inflates the sense that there is a much stronger cardiac effect than is actually present."

"The cardiac malformation observed with greatest frequency in this study was interventricular septal defect. The number of foetuses and litters with ventricular septal defects were 1, 1, 1 and 4 in the 0, 50, 150 and 450 mg/kg bw/day dose groups, respectively. Comparison of the **historical control** data shows that the heart findings (when presented on a percent individual and/or litter incidence basis) were slightly outside of the historical background range from 13 studies conducted during the same period. However, the disparity in values is a consequence of the small numbers of litters in the study report. If the data are displayed as a fraction (rather than a percentage), then the number of litters affected were 1/18 [6%], 1/12 [8%], 1/15 [7%], and 4/13 [31%] in the 0, 50, 150, and 450 mg/kg/day dose groups, respectively. The historical control range is 0/19-3/13 [23%]. Thus, the findings at the high dose are **barely outside of the historical control range**. Further, they were observed in conjunction with clear signs of maternal toxicity (reduced food consumption, body weight gains and increased clinical signs)."

[Vol. 3 Annex B.6.1, p. 645, emphasis added]. Comparing to "historical controls" rather than their own controls is an often-used trick to claim the results are not significant. In this last case, the cardiac malformations were even outside the "historical controls", so they decided to present as a fraction instead. Really, 4/13 isn't all that different from 3/13, is it?

One published study [57] and another abstract from a conference proceeding [58] were ranked category 1 (Reliable) and showed no endocrine disrupting effects for glyphosate.

One category 2 (Reliable With Restrictions) publication by Walsh et al. [59]showed that Roundup inhibited steroidogenesis by disrupting StAR protein expression. "Non-standard test systems, but publication meets basic scientific principles. However, surfactant blend in Roundup confounds results. Different effects of glyphosate alone and glyphosate formulations were observed. No conclusion can be drawn that the observed effects are result of glyphosate exposure" [Vol. 3 Annex B.6.1, p. 668]. They could find nothing wrong with it, but threw it out because it was based on a formulation, and not pure glyphosate.

A total of 18 peer-reviewed publications showing reproductive toxicity were ranked 3 (Not Reliable).

Paganelli et al. [60] reported endocrine disruption but was Not reliable because "Non-guideline study that is not sufficiently described for assessment. Inadequate positive and negative control experiments. Irrelevant routes of exposure and inappropriately high doses. Test system not adequate for human risk assessment" [Vol. 3 Annex B.6.1, p. 669]. Furthermore, "Multiple high quality toxicological studies and expert review panels consistently agree glyphosate is not a teratogen or reproductive toxicant. The author's justification for this research is flawed, providing no valid basis, other than an opinion, of an increase in the rate of birth defects in Argentina. Direct injection of frog embryos and through chicken shells do not reflect real world exposure scenarios to either environmental species or humans." It doesn't agree with their data so they are not going to consider it.

Richard et al. [61] reported endocrine disruption and toxic effects but was Not Reliable because. "Study design is insufficient for risk assessment of real exposure concentrations. Methodological deficiencies (no controls were included). Exceedingly high doses above the limit dose for this study type. Inappropriate test system for formulations containing surfactant; cytoxic membrane disruption potential of surfactants are well known for in vitro test systems. Excessive doses exceed typical in vitro limit doses. In vitro test system is inappropriate with surfactants" [Vol. 3 Annex B.6.1, p. 670].

Benachour et al. [62] reported that glyphosate is cytotoxic and potentially endocrine disrupting but was Not Reliable because, "Study report has several reporting deficiencies in the methods section (e.g. test conditions for the pH- and temperature dependent assay not reported). There is no information on the suitability of the used HEK 293 cell line for assessment of hormonal activity. Exceedingly high doses above the limit dose for this study type. Inappropriate test system for formulations containing surfactant. Study report has several reporting deficiencies in the methods section (e.g. test conditions for the pH- and temperature dependent assay not reported). There is no information on the suitability of the used HEK 293 cell line for assessment of hormonal activity. Exceedingly high doses above the limit dose for this study type. Excessive doses exceed typical in vitro limit doses. In vitro test system is inappropriate with surfactants" [Vol. 3 Annex B.6.1, p. 673].

Benachour et al. [63] reported that adjuvants like POEA change human cell permeability and amplify toxicity induced already by glyphosate through apoptosis and necrosis. Study found Not Reliable because, "Exceedingly high doses above the limit dose for this study type. Inappropriate test system for formulations containing surfactant; cytoxic membrane disruption potential of surfactants are well known for in vitro test systems. No positive controls were included" [Vol. 3 Annex B.6.1, p. 674].

Gasnier et al. [64] reported endocrine disruption but was Not Reliable because, “Due to reporting deficiencies (e.g. correlation between Gyphosate concentration used in toxicity tests and concentrations used in comet assay) assessment of results difficult. Exceedingly high doses above the limit dose for this study type. Inappropriate test system for formulations containing surfactant; cytoxic membrane disruption potential of surfactants are well known for in vitro test systems” [Vol. 3 Annex B.6.1, p. 675].

Clair et al. [65] reported endocrine disruption at low doses and testicular toxicity at high doses but was Not Reliable because, “Non-guideline in vitro test with methodological (i.e. no positive controls included) and reporting deficiencies (e.g. dose levels not always specified). Not relevant (Due to reliability. In addition, in vitro data do not reflect real in vivo exposure situations, and therefore not relevant for human risk assessment” [Vol. 3 Annex B.6.1, p. 676].

Hokanson et al. [66] reported that gene expression is altered in mammalian cells, by exposure to a variety of chemicals that mimic steroid hormones or interact with endocrine receptors or their co-factors. Study was Not Reliable because, “Not acceptable in vitro methods for test mixtures containing surfactant. Well documented study publication, but surfactants are inappropriate test substance in cell lines. Temporal altered gene expression is not a biomarker for toxicity, but rather, may be within the range of normal biological responses of homeostasis. In vitro cytotoxicity of surfactants, however, is a significant confounder in data interpretation. Data do not reflect real in vivo exposure situations, and therefore not relevant for human risk assessment purposes” [Vol. 3 Annex B.6.1, p. 678].

Yousef et al. [67] reported abnormal and dead sperm but was Not Reliable because, “Non-GLP, non-guideline study with major reporting deficiencies. Dose-levels poorly defined as 1/10 and 1/100 LD50. Purity of the test substances, source of animals, environmental conditions, mortality and clinical signs not reported. No testis and epididymis weights were determined or reported and no histopathological examination conducted. In addition, stability and homogeneity assessment of test substance preparations were not done or not reported. Rabbits have low body weights at study start, suggesting impaired health status. Not relevant (Due to low confidence in study conduct and the inadequacy of reporting.)” [Vol. 3 Annex B.6.1, p. 679].

Daruich et al. [68] reported maternal exposure to agrochemicals during pregnancy induces a variety of functional abnormalities. Study was Not Reliable because, “Basic data given, however, the study is performed with methodological and reporting deficiencies (unknown exposure levels, only cytosolic enzymes measured, inappropriate controls, lack of consistent dose-response data). Not relevant (Due to reliability. In addition, study was performed with a glyphosate formulation (commercialised in Argentina) and not with glyphosate)” [Vol. 3 Annex B.6.1, p. 680].

Romano et al. [69] reported increase in testicles and decreased testosterone but was Not Reliable because, “Study with methodological and reporting deficiencies or conflicting findings (e.g., increased relative testicular weights, but decreased testosterone measurements, Relevant study type for investigating male reproductive endpoints, but questionable relevance of this specific study based on low reliability of data and interpretation. Not relevant for glyphosate (test material was a formulated product, not glyphosate)” [Vol. 3 Annex B.6.1, p. 681].

Romano et al. [70] reported maternal exposure to glyphosate disturbed the masculinization process and promoted behavioral changes and histological and endocrine problems in reproductive parameters. Study was Not Reliable because, “Non-guideline, non-GLP study meeting scientific principles. Unusual and short dosing regiment commencing towards the end of pregnancy (GD18, rather than GD6 as per OECD Test Guidelines 414) through post natal day 5. In vivo study with reporting deficiencies (detailed strain description, source of animals, housing conditions, no information if clinical signs were assessed, stability and homogeneity assessment of test substance preparations, no of male offspring

evaluated in individual tests evaluated)" [Vol. 3 Annex B.6.1, p. 682].

Arbuckle et al. [71] reported postconception exposures were generally associated with late spontaneous abortions but was Not Reliable because, "No information about exposure duration, used glyphosate products and application rates. No information, if the subjects used more than one pesticide. Not relevant (Study design is not suitable for assessment of glyphosate exposure)" [Vol. 3 Annex B.6.1, p. 684].

Savitz et al. [72] reported miscarriage and pre-term delivery increased but was Not Reliable because, "No information about exposure duration, used glyphosate products and application rates. No information, if the subjects used more than one pesticide. Due to study design and evaluation methods, study results are not reliable" [Vol. 3 Annex B.6.1, p. 685].

Garry et al. [73] reported neurobehavioral and birth defects observed but were Not Reliable because, "Epidemiological study with some methodological reporting deficiencies (selection of study subjects, no information about exposure duration, exposure concentration, pesticide use frequency)" [Vol. 3 Annex B.6.1, p 688].

Garry et al. [74] reported significant increases in testosterone levels in fall compared to summer and also elevated levels of follicle-stimulating hormone but was Not Reliable because, "Epidemiological study with some methodological reporting deficiencies (e.g. selection of control subjects/samples, no details of exposure). Documentation is insufficient for assessment" [Vol. 3 Annex B.6.1, p. 689.].

Bell et al. [75] reported fetal death due to congenital anomalies from pesticide exposure but was Not Reliable because, "Epidemoliogical study with methodological deficiencies (e.g. glyphosate was included in the pesticide class of phosphates, thiophosphates, phosphonates; no differentiation between single and multiple exposures)" [Vol. 3 Annex B.6.1, p. 690].

Aris et al. [76] reported serum GLYP and GLUF were detected in non-pregnant women and serum 3-MPPA and CryAb1 toxin were detected in pregnant women, their fetuses and non-pregnant women. Study was Not Reliable because, "Exact levels of PAGMF, glyphosate or AMPA in the diets were not determined. It is not clear if the measured concentrations could have been resulted from other exposure routes. Provides real life actual exposure concentrations in humans. Data are limited due to the absence of any information on applied pesticides, application rates, etc.)" [Vol. 3 Annex B.6.1, p. 691].

Benítez-Leite et al. [77] reported a positive association between exposure to pesticides and congenital malformations. Study was Not Reliable because, "Study design of epidemiological study for developmental toxicity insufficient for assessment, as well as methological and reporting deficiencies (no assessment to which pesticides / active substances the mothers were exposed, use frequency not specified, selection of control group after study period is questionable, no information on exposure situation of mother for this control group assessed, etc.). The exposure to several pesticides was assessed in general, but no pesticide or active substance, including glyphosate, was specified or assessed)" [Vol. 3 Annex B.6.1, p. 692].

Much of the RMS findings that glyphosate has no reproductive toxicity was based on the review by Williams et al. [26]. Amy Lavin Williams [78] works for Exponent, a consulting company. "Prior to joining Exponent, Dr. Williams attained the position of Principal Scientist at Noblis/Mitretek Systems, where she provided toxicological analysis and support to both government and commercial clients related to chemicals of concern for environmental clean-up, drug substances and excipients, veterinary pharmaceuticals, and crop-protection compounds. Dr. Williams also held the position of Scientific Program Manager at the International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI), where she directed a diverse set of projects related to the development and application of toxicology data in safety risk assessment."

Exponent [79] : “Our regulatory expertise includes regulatory consultants and scientists who have extensive experience dealing with U.S., EU, and global issues and regulations. **We assist chemical manufacturers, pesticide registrants, grower/commodity groups, and trade associations in dealing with issues that affect their ability to do business effectively.** Our regulatory consultants and scientists provide strategic advice concerning regulatory compliance. We specialize in resolving difficult pesticide and non-pesticide issues involving the U.S. EPA, state agencies such as California Department of Pesticide Regulation, the EU and its member states, and Codex Alimentarius. [emphasis added]”

Neurotoxicity

“Two neurotoxicity studies in rats have been provided by the GTF. The delayed neurotoxicity studies in chicken that were reported in the original DAR (1998, ASB2010-10302) were re-evaluated by the RMS and found not acceptable. Thus, these studies using either the active ingredient or the formulation should not be used any longer for risk assessment” [Vol. 3 Annex B.6.1, p. 694].

Acute (single dose-rat)

“Two females receiving 2000 mg/kg bw glyphosate acid showed subdued behaviour, decreased activity, hunched posture, sides pinched in, tip-toe gait and hypothermia on the day of administration. One of these animals died on the subsequent day. The other one together with an additional female which showed diarrhoea on the day of administration regained full recovery the subsequent day. One female receiving 500 mg/kg bw, was found dead approximately 6 h after administration. In the absence of any treatment-related clinical signs prior to death, and because no deaths were observed at the intermediate dose level of 1000 mg/kg bw, the death of this animal was considered not to be treatment related.”

13 weeks (rat)

“reduced growth and reductions in food utilisation for males. Comprehensive histopathological evaluation of the nervous system showed no evidence of any changes in the peripheral or central nervous system which could be attributed to administration of glyphosate acid.”

Two published studies showing neurotoxicity were “not assignable” and two were considered Not Reliable.

Barbosa et al. [80] reported an accidental exposure in a 54-yr old male: skin lesions; one month later Parkinson's. Study was Not assignable because, “Medical case report, single incident (Data are limited due to the absence of any information on purity and application concentrations of glyphosate formulation, as well as co-formulations.)” [Vol. 3 Annex B.6.1, p. 707].

Wang et al. [81] reported that a 44 yr old woman developed Parkinson's after 3-year exposure working at chemical plant. Study was Not assignable because, “Medical case report, single incident” [Vol. 3 Annex B.6.1, p. 708].

Astiz et al. [82] reported oxidative stress in liver and brain but was Not Reliable because, “Unsuitable test system (i.p exposure route is not relevant for human exposure). No information on purities of test substances used. Small group size (4 males/dose group), reporting deficiencies Not relevant (intraperitoneal injection is a non-relevant route of exposure for humans) Statistically significant effects were noted for brain tissue endpoints in the substantia nigra and cerebral cortex. However, there is a lack of biological plausibility for brain exposures to glyphosate, given the necessity to pass the blood-brain barrier and the known rapid elimination kinetics of this polar molecule via urine” [Vol. 3 Annex B.6.1, p. 709].

Gui et al. [83] reported that glyphosate induced cell death via autophagy pathways in addition to

activating apoptotic pathways. Study was Not Reliable because, “Documentation insufficient for assessment (not clearly stated dose levels and duration of exposure, as well as treatment conditions for all tests. In addition, tested doses were much higher than real in vivo concentrations). Not relevant (Due to reliability)” [Vol. 3 Annex B.6.1, p. 710].

Salivary gland

“Both isoproterenol and glyphosate induced significant enlargement of the salivary glands, glyphosate having much greater effect than isoproterenol. The parotid was most affected. Propranolol inhibited the effect of both substances on salivary gland weight but not completely in the case of glyphosate. Microscopically, similar changes were induced by glyphosate and isoproterenol consisting of cytoplasmic basophilic change, fine vacuolation and swelling of acinar cells resulting in a relative reduction in the number of ducts present. Glyphosate-treated animals were most severely affected. Propranolol, however, clearly protected the rats from the more severe lesions. Cytoplasmic alteration of the submandibular gland was more subtle and histologically detectable only in glyphosate-treated animals. However, electron microscopy elucidated an effect of isoproterenol on this gland, too. It could not be determined if the serous or mucous glandular acini were selectively affected by glyphosate. No changes were seen in the sublingual glands examined from any group demonstrating target specifity of glyphosate- and isoproterenol-associated lesions to those salivary glands which are mainly innervated by adrenergic fibers. The authors assume that effects of glyphosate on salivary glands were due to an adrenergic mechanism. The biological significance of this finding is unkown” [Vol. 3 Annex B.6.1, p. 733].

Farm Animals

Four unpublished, Monsanto-sponsored studies on farm animals were submitted; 2 on goat, 2 on cows [Vol. 3 Annex B.6.1,pp. 757-781].

Goats (single dose):

All of the animals in the two highest dose groups died. Observed signs of toxicity: colic, diarrhea, taxia and weakness. These signs of toxicity were observed at most dosage levels above 1400 mg/kg bw. “Additional symptoms suggestive of central nervous system involvement were observed at dosages of 4290 mg/kg bw and above, including tremors, convulsions, and unusual behaviour.”

In detail:

Clinical signs of goats that died included decreased food consumption, abdominal distress, ataxia and, shortly prior to death, recumbency. One goat that died and one surviving goat each displayed an unusual collapsing syndrome of apparent neurological origin approximately 2 days after receiving MON 0139 while other goats displayed various other neurological signs.

One surviving goat developed extensive ulceration of the tongue and oral mucosa.

Other observations in dosed groups: minimal fat stores, bloat, gallbladder edema, pulmonary edema, depressed demeanor, ataxia, labored breathing, diarrhea, thirst, nystagmus, pneumonia, pericarditis (inflammation of the heart membrane), rumen haemorrhage, chronic hepatitis, hepatic atrophy, macerated fetus, endometritis, fetal death, renal atrophy.

Cows (7 days): All animals in the highest dose group and one out of three in the next highest goups died.

Observations: diarrhea, decreased feed intake, nasal discharge, foamy salivation, head tremors, belligerency, whole-body tremors, ataxia (loss of muscle coordination), head pressing, kicking at

imaginary objects, apparent visual impairment, convulsions, falling, depression, recumbency, increased respiratory effort, depression, weakness,dehydration, loss of weight and signs indicative of gastrointestinal irritation enlarged kidney, enlarged liver, dermatitis, difficulty breathing, epicardial petechiae, petechiae of spleen, trachea mucosa and pleura, heart valve hemocyst, congested intestine, gall bladder distension, gall bladder, congested liver, congested spleen, spleen, liver scars, esophagus erosion, mottled liver, bladder petechiae (blood spots).

“Krüger et al. [84] reported the abundance of glyphosate in the urine of a total of 240 cows from Denmark. It is a reasonable assumption that urinary excretion of glyphoate was due to dietary exposure and, thus, detection of glyphosate in the urine of cattle is not surprising. Residues of glyphosate may occur in feedstuffs for ruminants and, so far the MRLs are not exceeded, are allowed and of no concern” [Vol. 3 Annex B.6.1, p. 782].

“A number of papers has [sic] been published recently in which a possible causal link of glyphosate exposure and subsequent Clostridium botulinum (C. botulinum) overgrowth with a new disease in cattle is suggested” [Vol. 3 Annex B.6.1, p. 785]. Rodloff and Krüger [85] hypothesised that an emerging new disease in cattle but also symptoms in a small number of farmers might be caused by Clostridium botulinum. This animal disease of so far unknown etiology and pathogenesis was reported to have occurred from the late 1990ies onwards in cattle mainly from some parts of Germany but, according to the authors, cases had been observed also in France, the Netherlands, and the U.K. even though references were not given. Clinical signs in cattle are predominately seen in the perinatal period and comprise indigestion with alternating constipation and diarrhea, apathy, ataxia, paralysis, retracted abdomen, breathing difficulties, a decrease in milk yield, and death. In some farmers taking care of affected herds, symptoms such as dizziness, weakness, fatigue, blurred vision, nausea, and difficulties to speak, to swallow and to breathe have been occasionally reported” [**note:** same symptoms as the industry-sponsored toxicology reports on goats and cows!] [Vol. 3 Annex B.6.1, p. 784].

“The scientific background of this assumption is the herbicidal mode of action of glyphosate. In plants, the enzyme 5-enolpyruvylshikimic acid-3-phosphate synthase (EPSP synthase) is inhibited resulting in a lack of formation of aromatic amino acids by the shikimate pathway that is common in the plant kingdom but not does not occur in animals. However, this pathway is operative in most bacteria and yeast and many protozoan species. Thus, an impact of glyphosate on microflora, e.g., in the intestines, is at least conceivable.” [Vol. 3 Annex B.6.1, p. 784].

RMS conclusion: “In itself, this paper is adequate to suggest a scientific hypothesis, based on some data that might require further research. However, no causal relationship between a new disease in cattle and C. botulinum has been established.” [Vol. 3 Annex B.6.1, p. 784].

“In a similar paper, Krüger et al. [86] reported the abundance of (different types) of the micro-organism C. botulinum itself in 44 out of 196 bovine fecal samples (22.5%) and in 17 out of 77 human fecal samples (22%) but also in silages (9 / 21 = 47%), concentrate feed specimens (4 / 14 = 28.6%)” [Vol. 3 Annex B.6.1, p. 785]

Conclusion by RMS:

“The findings rather point to ubiquitious occurrence of C. botulinum but are not suitable to prove a causal relationship of its abundance to clinical signs or symptoms” [Vol. 3 Annex B.6.1, p. 785].

“Krüger et al. [87] reported that glyphosate (analytical grade) and the herbicide Roundup UltraMax® containing 450 glyphosate/mL was able to suppress this antagonizing of effect of Enterococcus species on C. botulinum in vitro” [Vol. 3 Annex B.6.1, p. 785].

Conclusion by RMS:

“This data suggests a different susceptibility of E. faecalis and C. botulinum to cytotoxic effects of glyphosate and a glyphosate-based herbicide in vitro. ... Thus, the possible impact of glyphosate (herbicides) on bacteria due to inhibition of the enzyme EPSP was somehow confirmed in vitro but there is no health concern and no impact on realistic risk assessment.” [Vol. 3 Annex B.6.1, p. 785].

“A different toxicity of Roundup UltraMax® to various microbial species was also observed by Shehata et al. [88] who measured the effect of different concentrations on 23 bacterial species and strains mostly of chicken origin and also on sporulated Eimeria tenella (i.e., a protozoon in poulty) oocytes in vitro. In general, the authors found lower minimum inhibitory concentrations for beneficial bacteria whereas, in contrast, some pathogenic germs such as Clostridium perfringens or several Salmonella species appeared much less sensitive with growth inhibition seen only at the highest tested concentration of 5 mg/mL. With regard to Eimeria tenella, the threshold for an effects was around 0.3 mg/mL with a clear effect to be seen at 0.6 mg/mL.” [Vol. 3 Annex B.6.1, p. 786]

Conclusion by RMS:

“Different cytototoxicity of a glyphosate-based herbicide to micro-organisms was confirmed once more and might be due to either the active ingredient or, e.g., a surfactant. (It is not known whether a surfactant was contained.) However, antibiotic activity of the herbicide (expressed in the minimum inhibitory concentrations) was lower than that of known antibiotics that are used in veterinary medicine. Even the lowest effect concentrations in this study were by far higher than the expected glyphosate concentrations in poultry feed (GTF, 2013; ASB2013-11007) and, thus, must be considered unrealistically high. Furthermore, in vitro exposure of selected indivdual species and strains to a herbicide might be not a good model for complex interactions in GIT of poultry when residues are ingested” [Vol. 3 Annex B.6.1, p. 786] .

“To conclude, a link of glyphosate residues in ruminants diet to a new disease in cattle has not been established and is not likely.” [Vol. 3 Annex B.6.1, p. 786].

Eleven more peer-reviewed papers finding harmful effects of glyphosate not classified elsewhere were rejected as Not Reliable: Clair et al. [89], Mesnage et al. [90], Benedetti et al. [91], Axelrad et al. [92], Heu et al., [93 & 94], Marc et al. 95-98] and Robert et al. [99].

There was no mention whatsoever of the Carman pig study or the Samsel & Seneff review paper.

Summary

According to the EPA [100], there were 271 incidences of glyphosate poisoning reported covering the period from 2002-2009. From these 271 reports there were: 4.8% gastrointestinal (diarrhea, abdominal cramps & stomach pain); 29.5% dermal; 10.3% upper respiratory (shortness of breath, coughing, asthma, bronchitis, congestion & pneumonia); 36.2% neurological (shaking, loss of coordination, tingling, neuropathy, ataxia & numbness); 0.36% cardiovascular; 14.4% ocular; 3.7% combined effects and 0.7% had no symptoms.

All of these symptoms and more were observed in the industry's own studies. Yet they make up a number that is supposedly safe. They **know** that glyphosate is toxic and that it causes all of these problems. The BfR and EFSA are simply rubber-stamping the industry's claims, burying their collective heads in the sand (or somewhere else).

Does anyone know what we are now exposed to via air, water and food? How about exposure over 20 years? We are beginning to see these long-term effects.

The bigger issue is how we came to accept the common practice of taking known chemical poisons and

feeding, injecting, and rubbing it into the eyes and skin of rabbits, dogs, guinea pigs, mice and rats to determine the level of harm. Then we declare the chemical poisons harmless to us at something less than that level. How did the world become so insane that this is okay with anyone?

[1] Announcement of RAR finalized on BfR website: http://www.bfr.bund.de/en/the_bfr_has_finalised_its_draft_report_for_the_re_evaluation_of_glyphosate-188632.html

[2] Glyphosate Task Force, http://www.glyphosate.eu/

[3] Renewal Assessment Report on glyphosate (2014)

Vol. 1. Report & proposed decision, 174 pages. Report and Proposed Decision. (Summary)
Vol. 2 Annex A. List of tests & studies, 251 pages.
Vol. 3 Annex B.1. Identity, 12 pages. (Molecular structure and description)
Vol. 3 Annex B.2. Physical & chemical properties, 41 pages.
Vol. 3 Annex B.3. Data on application and further information, 30 pages. (Application rate, storage & handling)
Vol. 3 Annex B.4. Proposals for the classification and labelling, 3 pages.
Vol. 3 Annex B.5. Methods of analysis, 103 pages. (Analytical methods for determination of active substance, impurities and residues)
Vol. 3 Annex B.6.1. Toxicology and metabolism, 947 pages. (Animal and human toxicology)
Vol. 3 Annex B.7. Residue data. 965 pages. (Crop residues)
Vol. 3 Annex B.8. Environmental fate and behaviour, 361 pages.
Vol. 3 Annex B.8 (Appendix). Evaluation of open literature regarding environmental fate and behaviour, 323 pages.
Vol. 3 Annex B.9. Ecotoxicology, 314 pages. Non-targeted plants, birds, fish and other creatures.
Vol. 3 Annex B.9 (Appendix). Evaluation of peer-reviewed literature on ecotoxicology, 201 pages.
List of endpoints, 77 pages.
List of information, tests and studies which are considered as relied upon by the RMS for evaluation, 143 pages.

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