Glyphosate Information.

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Contents

1. Preface: The present day discourse on toxic effects of Glyphosate

1.1. The Case of Don Huber, emeritus Prof. Perdue University:

It seems that the correlation between diseases in extreme monocultures of glyphosate tolerant crops has some merits, but the correlation to glyphosate is certainly not clear, it has to do with bad agricultural management of gigantic monocultures, see the controversy between Broer (Broer, I, et al., 2009, Broer, I, et al., 2011) and Taube [1] (Taube, F, et al., 2011), which, according to an oral

[1] **Broer, I., Busch, R.J., Jung, C., Ordon, F., Qaim, M., Reinhold-Hurek, B., Sonnewald, U., von Tiedemann, A., Moehring, C., Schmitz-Moeller, P., & Deutsche Forschungsgemeinschaft (2009)**
Gruene Gentechnik, Deutsche Forschungsgemeinschaft pp 56 (Report)
http://www.botanischergarten.ch/Regulation/DFG-Broschuer-Gruene-Gentechnik-2009.pdf

Broer, I., Jung, C., Ordon, F., Qaim, M., Reinhold-Hurek, B., Sonnewald, U., & von Tiedemann, A. (2011)
Response to the criticism by Taube et al. in ESE 23:1, 2011, on the booklet "Green Genetic Engineering" published by the German Research Foundation (DFG). Environmental Sciences Europe, 23, 1, pp 16

communication by Inge Broer, has now developed into a constructive dialogue. It is not justified, how Prof. em. Don Huber is talking in an alarmist way about unknown microbes etc. and links it to Glyphosate application directly – for his unknown diseases he has not only no data presented, but also he has not even really started the project of which he is trumpeting out results. The publications Don Huber authored or co-authored which are available from Web of Science: (Fernandez, MR, et al., 2009), (Fernandez, MR, et al., 2008), (Saes Henrique, et al., 2009).

Fernandez, M.R., Zentner, R.P., Basnyat, P., Gehl, D., Selles, F., & Huber, D.M. (2009)
Glyphosate associations with cereal diseases caused by Fusarium spp. in the Canadian Prairies. European Journal of Agronomy, 31, 3, pp 133-143
http://www.sciencedirect.com/science/article/pii/S1161030109000689 AND
http://www.ask-force.org/web/HerbizideTol/Fernandez-Glyphosate-Associations-2009.pdf

Fernandez, M.R., Huber, D., Basnyat, P., & Zentner, R.P. (2008)
Impact of agronomic practices on populations of Fusarium and other fungi in cereal and noncereal crop residues on the Canadian Prairies. Soil & Tillage Research, 100, 1-2, pp 60-71
<Go to ISI>://WOS:000259833600007
AND http://www.ask-force.org/web/HerbizideTol/Fernandez-Impact-Agronomic-Practices-2008.pdf

Saes Henrique, Zobiole Luiz, de Oliveira, R., Huber Morgan Don, Constantin Jamil, de Castro Cesar, de Oliveira Fabio, & de Oliveira Adilson (2009)
Glyphosate reduces shoot concentrations of mineral nutrients in glyphosate-resistant soybeans. Plant and Soil, 328, 1, pp 57-69
http://dx.doi.org/10.1007/s11104-009-0081-3
AND http://www.ask-force.org/web/HerbizideTol/Henrique-Saes-Zobiole-Glyphosate-Reduces-2009.pdf

Huber, D.M. (2007)
Strategies to ameliorate glyphosate immobilization of Mn and its impact on disease. Phytopathology, 97, 7, pp S168-S168
<Go to ISI>://000247470001444
AND http://www.ask-force.org/web/HerbizideTol/Huber-Strategies-Ameliorate-2007.pdf

Huber, D.M., Cheng, M., & Winsor, B. (2005)
Association of severe Corynespora root rot of soybean with glyphosate-killed ragweed. Phytopathology, 95, 6, pp S45-S45
<Go to ISI>://000202991400275 AND
http://www.ask-force.org/web/HerbizideTol/Huber-Association-severe-Corynespora-2005.pdf

Johal, G.S. & Huber, D.M. (2009)
Glyphosate effects on diseases of plants. European Journal of Agronomy, 31, 3, pp 144-152
http://www.sciencedirect.com/science/article/pii/S1161030109000628 AND
http://www.ask-force.org/web/HerbizideTol/Johal-Glyphosate-Effects-2009.pdf

And an example of a blog (Zerbe Leah, 2011) where Don Huber is cited, supported by the fundamentalist lay publisher Jeremy Smith (about the low scientific quality of Jeremy Smith's statements, a fervent supporter of levitation, see http://academicsreview.org/)

"Huber, one of the world's top researchers of glyphosate, says we're in "epidemic mode" right now in terms of plant diseases induced by Roundup use. These plant diseases could affect humans and livestock eating the diseased plants, too. As Jeffrey Smith, founder of the

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http://www.enveurope.com/content/23/1/16 AND
http://www.ask-force.org/web/Regulation/Broer-Stellungsname-DFG-2011.pdf

Taube, F., Krawinkel, M., Susenbeth, A., & Theobald, W. (2011)
The booklet "Genetically modified crops" published from the German Research Foundation, does not meet the given claim. Environmental Sciences Europe, 23, 1, pp 1
http://www.enveurope.com/content/23/1/1 AND
http://www.ask-force.org/web/Regulation/Taube-DFG-Genuegt-Nicht-2011.pdf

Institute for Responsible Technology, points out, some of the fungi that thrive on glyphosate produce harmful toxins that can enter the food chain, either in human food or animal feed. Smith cites a UN Food and Agriculture Organization report that links one such fungus, Fusarium, in the food chain to certain cancers, a blood disorder, and infertility in animals. Smith says USDA researchers have found a 500 percent increase in Fusarium root infection when glyphosate is used on Roundup Ready soybeans. (This toxin can also appear in corn, wheat, and other crops.) "Like glyphosate, Fusarium toxins accumulate in our bodies, too," says Huber." (Zerbe Leah, 2011)

There is not a shred of evidence for those scaremonger statements cited above, but lots of people are unfortunately ready to buy such pseudoscience. But the scientific community had up to now no opportunity to discuss those claims on a factual basis.

The clear reply of his former Perdue University colleagues : (Camberato, J, et al., 20110224)

Camberato, J., Castell, S., Goldsborough, P., Johnson, B., Wise, K., & Woloshuk, C. (20110224)
Glyphosates Impact on Field Crop Prodution and Disease Development. Purdue Extension Weed Science, 2, pp 4
http://www.btny.purdue.edu/weedscience/2011/GlyphosatesImpact11.pdf AND
http://www.ask-force.org/web/Regulation/Camberato-Glyphosates-Impact-Huber-Rebuttal-Purdue-2011.pdf AND
edited with full text links of citations http://www.ask-force.org/web/HerbizideTol/Camberato-Glyphosates-Impact-Purdue-2011-ka.pdf

Selected sentences:

"The claim that herbicides, such as glyphosate, can make plants more susceptible to disease is not entirely without merit. Research has indicated that plants sprayed with glyphosate or other herbicides are more susceptible to many biological and physiological disorders." [see section below]
"Despite the potential for herbicides to increase disease levels in certain plants, plant pathologists have NOT observed a widespread increase in susceptibility to plant diseases in glyphosate-resistant corn and soybean."
„Although some research indicates there is an increase in disease severity on plants in the presence of glyphosate, it does NOT necessarily mean that there is an impact on yield."
"Overall, the claims that glyphosate is having a widespread effect on plant health are largely unsubstantiated."

More doubts on the unscientific campaign of Don Huber and helping activists against the use of glyphosate can be seen on the website of GMO-Safety (GMO-Safety, 2011):

GMO-Safety (2011)
Electronic Source: Is glyphosate dangerous? Anti-herbicide campaign on shaky ground, debate about GM crops with herbicide resistance, published by: Ministry of Environment Germany http://www.gmo-safety.eu/news/1358.dangerous-glyphosate.html
AND http://www.ask-force.org/web/HerbizideTol/Glyphosate-Huber-GMO-Safety-20111017pdf.pdf

There are some papers demonstrating that Glyphosate susceptible plants weakened by Glyphosate show slightly higher infection rates by certain soil fungi (Babiker, EM, et al., 2011), (Johal, GS & Rahe, JE, 1984, Johal, GS & Rahe, JE, 1988, Johal, GS & Rahe, JE, 1990, Johal, GS & Huber, DM, 2009).

Despite the moderate potential for herbicides to increase disease levels in certain plants, plant pathologists have NOT observed a widespread increase in susceptibility to plant diseases in glyphosate-resistant corn and soybean.

A recent lab study (Li Q, LM, Zhang Q, Liu S, Ge D, Yin R, Xi M, You Z, 20130724) suggests that Glyphosate and AMPA inhibit cancer cell growth through inhibiting intracellular glycine synthesis.

Li Q, L. M., Zhang Q, Liu S, Ge D, Yin R, Xi M, You Z (20130724), Glyphosate and AMPA inhibit cancer cell growth through inhibiting intracellular glycine synthesis, Drug Design, Development and Therapy, 2013:7, pp. 635 - 643, http://dx.doi.org/10.2147/DDDT.S49197 AND
http://www.dovepress.com/glyphosate-and-ampa-inhibit-cancer-cell-growth-through-inhibiting-intr-peer-reviewed-article-DDDT AND
http://www.ask-force.org/web/HerbizideTol/Li-Glyphosate-AMPA-Inhibit-Cancer-20130723.pdf

"Glycine is a nonessential amino acid that is reversibly converted from serine intracellularly by serine hydroxymethyltransferase. Glyphosate and its degradation product, aminomethylphosphonic acid (AMPA), are analogs to glycine, thus they may inhibit serine hydroxymethyltransferase to decrease intracellular glycine synthesis. In this study, we found that glyphosate and AMPA inhibited cell growth in eight human cancer cell lines but not in two immortalized human normal prostatic epithelial cell lines. AMPA arrested C4-2B and PC-3 cancer cells in the G1/G0 phase and inhibited entry into the S phase of the cell cycle. AMPA also promoted apoptosis in C4-2B and PC-3 cancer cell lines. AMPA upregulated p53 and p21 protein levels as well as procaspase 9 protein levels in C4-2B cells, whereas it downregulated cyclin D3 protein levels. AMPA also activated caspase 3 and induced cleavage of poly (adenosine diphosphate [ADP]-ribose) polymerase. This study provides the first evidence that glyphosate and AMPA can inhibit proliferation and promote apoptosis of cancer cells

but not normal cells, suggesting that they have potentials to be developed into a new anticancer therapy." (Li Q, LM, Zhang Q, Liu S, Ge D, Yin R, Xi M, You Z, 20130724)

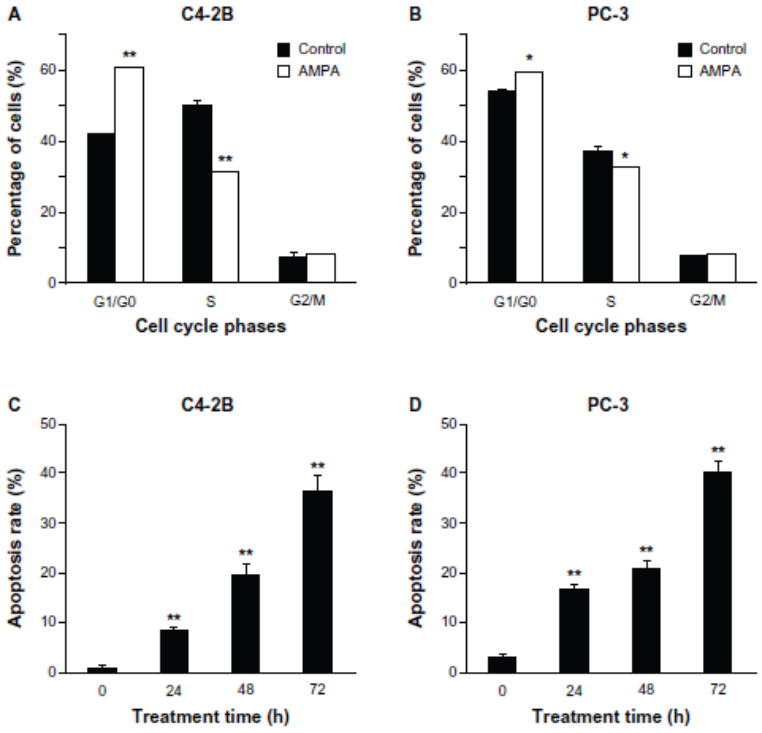

Figure 1 AMPAinhibits entry into the Sphase of cell cycle and increases apoptosis.

Notes: C4-2B and PC-3 cells were treated with or without 50 mM AMPAfor 24 hours (**A** and **B**) or 0, 24, 48, and 72 hours (h) (**C** and **D**). Percentages of the cells in G1/G0, S, and G2/M phases of cell cycle were determined using propidium iodide staining and flow cytometry analysis (**A** and **B**). Apoptosis rates were determined using Annexin-V FITC Conjugate and propidium iodide double staining and flow cytometry analysis (**C** and **D**). Data represent the mean ± SEM obtained from three independent experiments. *P , 0.05 and **P , 0.01, compared with the control group. **Abbreviations:** AMPA, aminomethylphosphonic acid; FITC, Fluorescein isothiocyanate; SEM, standard error of the mean.

1.2. Additional controversies on Glyphosate related to supposed toxicity

An additional glimpse to the battle field of the Glyphosate pseudo-debate of the opponents shows that the discussion is still going on, and the GM opponents especially in Europe are very successful, for instance with the "renowned University Professor" Antoniou, touring the whole world, just as Huber (wonder where they get it funded from), he recently published a veritable Anti-Glyphosate bible distributed on numerous websites of GM opponents:

Antoniou, M., Paulo Brack,, Andrés Carrasco, J.F., Mohamed, Habib, P.K., Carlo Leifert,, & Rubens Onofre Nodari, W.P. (2010)
GM Soy, Sustainable? Responsible? A summary of scientific evidence showing that genetically modified (GM) soy and the glyphosate herbicide it is engineered to tolerate are unsustainable from the point of view of farming, the environment, rural communities, animal and human health, and economies © 2010 Copyright by GLS G© 2010 Copyright by GLS Gemeinschaftsbank eG and ARGE Gentechnik-freiemeinschaftsbank eG and ARGE Gentechnik-frei pp 37 (Report)
http://environmentportal.in/files/gmsoy_sust_respons_full_eng_v12.pdf AND
http://www.ask-force.org/web/HerbizideTol/Antoniou-GM-Soy-Sustainable-Responsible-2010.pdf

In addition, it is mainly the Carrasco school cranking out more flawed papers, roughly the same allegations already brought forward by Don Huber:

Carrasco, A.E. (2010)
Reply to the Letter to the Editor Regarding Our Article (Paganelli et al., 2010). Chemical Research in Toxicology, 24, 5, pp 610-613
http://www.ask-force.org/web/HerbizideTol/Carrasco-Reply-to-the-Letter-Paganelli-2010.pdf

Carrasco, A.E. (2011)
Glyphosate: part of a eugenics model? Salud Colectiva, 7, 2, pp 129-133
http://www.ask-force.org/web/HerbizideTol/Carrasoc-Glifosato-Modelo-Eugenesico-2011.pdf

Paganelli, A., Gnazzo, V., Acosta, H., Lopez, S.L., & Carrasco, A.E. (2010)
Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling. Chemical Research in Toxicology, 23, 10, pp 1586-1595
http://www.ask-force.org/web/HerbizideTol/Paganelli-Glyphosate-Based-Effects-2010.pdf

the rebuttals to the above paper of Paganelli:

Saltmiras, D., Bus, J.S., Spanogle, T., Hauswirth, J., Tobia, A., & Hill, S. (2011)
Letter to the Editor Regarding the Article by Paganelli et al. Chemical Research in Toxicology, 24, 5, pp 607-608
http://www.ask-force.org/web/HerbizideTol/Saltmiras-Letter-Paganelli-2011.pdf

Multiple high quality toxicological studies and expert review panels consistently agree glyphosate is not a teratogen or reproductive toxicant: The GLP studies that Paganelli et al. infer as untrustworthy "industry-funded studies" have been exhaustively reviewed by multiple government scientific regulators, often comprising academic expert scientists and all of which have strongly supported the conclusions put forth in those studies. Glyphosate does not cause adverse reproductive effects in adult animals or birth defects in offspring of these adults exposed to glyphosate, even at very high doses. These conclusions are based on multiple studies in laboratory animals that have been conducted to examine the potential for multigenerational and teratogenic effects. These studies have been repeated by different companies at different laboratories across the globe over the last 30 or more years, with consistent results demonstrating that glyphosate does not pose the concerns raised by the authors. Regulatory authorities and independent experts who have documented this position include WHO/FAO,1 U.S. EPA,2 the European Commission,3 and Williams et al.4

Mulet, J.M. (2011)
Letter to the Editor Regarding the Article by Paganelli et al. Chemical Research in Toxicology, 24, 5, pp 609-609
http://dx.doi.org/10.1021/tx200077h AND http://www.ask-force.org/web/HerbizideTol/Mulet-Letter-Paganelli-2011.pdf

Palma, G. (2011)
Letter to the Editor Regarding the Article by Paganelli et al. Chemical Research in Toxicology, 24, 6, pp 775-776
http://dx.doi.org/10.1021/tx200086y AND http://www.ask-force.org/web/HerbizideTol/Palma-Letter-Paganelli-2011.pdf

The Seralini research group published a long-term study with lots of methodological errors about a transgenic maize : in this paper they also blame it's transgenic herbicide tolerance for negative effects in rat experiments. The study has been criticized by more than 30 research organizations and also by the European Food Safety Agency with strong words, rejects to accept the conclusions. The original paper : (Seralini Gilles-Eric, et al., 20120918), the two most comprehensive rebuttals : (Arjó, G, et al., 2013, Jany Klaus, 2013), much has been written pro and contra the study, which in the view of the overwhelming majority of the community of toxicology scientists has been totally refuted, a bibliography of some 700 items was collected by the author, which needs to be updated for the last 5 months.

2. Some Basic Publications and Reports of Glyphosate Applications and Toxicity

2.1. The Development of Glyphosate and the first US Government Evaluations of Glyphosate

Glyphosate was discovered in its full application value by John L. Franz [2] who published the invention in 1991 in Plant Physiology as senior author:

Logusch, E.W., Walker, D.M., McDonald, J.F., & Franz, J.E. (1991)
INHIBITION OF PLANT GLUTAMINE SYNTHETASES BY SUBSTITUTED PHOSPHINOTHRICINS. Plant Physiology, 95, 4, pp 1057-1062
http://www.ask-force.org/web/HerbizideTol/Logusch-Inhibition-Glutamin-Phosphinothricins-1991.pdf

From the Monsanto Backgrounder on the History 2005 (Monsanto, 2005a): the original Roundup herbicide refers to the Roundup agricultural herbicides (also known as MON2139), which contained the active ingredient glyphosate (as the isopropylamine salt) water and surfactant (polyoxyethylene-alkylamine or POEA). See also (Federal Register, 2000) for more details of the numerous safety assessment experiments listed. Here only an excerpt on major official safety assessment results:

"1. Dietary exposure from food and feed uses. Tolerances have been established (40 CFR 180.364) for the residues of glyphosate, in or on a variety of food commodities. Tolerances are established for cattle, hog, horse and sheep kidney at 4.0 ppm and liver at 0.5 ppm. Tolerance levels for residues of glyphosate at 0.1 ppm for egg and poultry meat and 1.0 ppm for poultry meat byproducts were proposed by IR-4. Risk assessments were conducted by EPA to assess dietary exposures from glyphosate in food as follows:

2. Acute exposure. Acute dietary risk assessments are performed for a fooduse pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1–day or single exposure. An acute dietary endpoint and dose was not identified for glyphosate. A review of the rat and rabbit developmental studies did not provide a dose or endpoint that could be used for acute dietary risk purposes. Additionally, there were no data requirements for acute or subchronic rat neurotoxicity studies since there was no evidence of neurotoxicity in any of the toxicology studies at very high doses and glyphosate lacks a leaving group.

3. Chronic exposure. In conducting this chronic dietary risk assessment the Dietary Exposure Evaluation Model (DEEM¢) analysis evaluated the individual food consumption as reported by respondents in the USDA 1989–1992 nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The following assumptions were made for the chronic exposure assessments: The chronic dietary exposure analysis from food sources was conducted using the reference dose (RfD) of 2.0 mg/kg/day.
The RfD is based on the maternal NOAEL of 175 mg/kg/day from a rabbit developmental study and an uncertainty factor of 100 (applicable to all population subgroups). The DEEM¢ analysis assumed tolerance level residues and 100% crop treated in/on all commodities with an existing or proposed glyphosate tolerance.

4. Cancer. There is no evidence of carcinogenic potential" (Federal Register, 2000)

Under www.regulations.gov you find under the keyword Glyphosate on June 13, 2012 some 20336 documents.

The original registration of Glyphosate 1974:
The EPA re-registration of Glyphosate and earlier documents (EPA Glyphosate-Summary, 2009, EPA reregistration, 1993) also confirm that there are no problems with glyphosate in agricultural applications:

The detailed statements on safety assessment follow the same pattern as the later publication of Williams, Kroes and Munro (Williams, GM, et al., 2000). The original conclusion text, p. 7 of the EPA re-registration (EPA reregistration, 1993)

[2] Wikipedia of John F. Franz http://en.wikipedia.org/wiki/John_E._Franz

Regulatory Conclusion

The use of currently registered pesticide products containing the isopropylamine and sodium salts of glyphosate in accordance with the labeling specified in this RED will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

EPA reregistration (1993)

RED Reregistration Eligibility Decision Document Glyphosate (eds EPA Environment Protection Agency). EPA, Washington DC. http://www.epa.gov/pesticides/reregistration/glyphosate/ AND http://www.ask-force.org/web/HerbizideTol/EPA-RED-Decision-glyphosate-1993.pdf AND about tolerances http://www.epa.gov/fedrgstr/EPA-PEST/1997/April/Day-11/p9231.htm

EPA Glyphosate-Summary (2009)

Glyphosate Summary Document: Registration Review: Initial Docket EPA-HQ-OPP--2009-0361, June 2009, Case Nr. 0178 (eds EPA), pp. 16. EPA, Washington DC. www.regulations.gov AND http://www/ask-force.org/web/HerbizideTol/EPA-Glyphoste-Summary-HQ-OPP-2009-0361-0003-2009.pdf AND http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2009-0361 AND http://www.epa.gov/fedrgstr/EPA-PEST/2009/July/Day-22/p17404.pdf AND http://www.ask-force.org/web/HerbizideTol/EPA-Registration-Review-Glyphosate-2009.pdf

Lots of interesting authoritative references are demonstrated repeatedly, that glyphosate use is not problematic from the point of view of toxicology.

A major publication is the "long forgotten" and unfortunately rarely cited review of Williams et al. (Williams, GM, et al., 2000).

Williams, G.M., Kroes, R., & Munro, I.C. (2000)

Safety Evaluation and Risk Assessment of the Herbicide Roundup and Its Active Ingredient, Glyphosate, for Humans. Regulatory Toxicology and Pharmacology, 31, 2, pp 117-165
http://www.sciencedirect.com/science/article/B6WPT-45C0WDC-1/2/28ae5dd7a84837f8a2b1f085177834c0 AND http://www.ask-force.org/web/HerbizideTol/Williams-Safety-Evaluation-Risk-Assessment-RR-2000.pdf

"Reviews on the safety of glyphosate and Roundup herbicide that have been conducted by several regulatory agencies and scientific institutions worldwide have concluded that there is no indication of any human health concern. Nevertheless, questions regarding their safety are periodically raised. This review was undertaken to produce a current and comprehensive safety evaluation and risk assessment for humans. It includes assessments of glyphosate, its major breakdown product [aminomethylphosphonic acid (AMPA)], its Roundup formulations, and the predominant surfactant [polyethoxylated tallow amine (POEA)] used in Roundup formulations worldwide.

The studies evaluated in this review included those performed for regulatory purposes as well as published research reports. The oral absorption of glyphosate and AMPA is low, and both materials are eliminated essentially unmetabolized. Dermal penetration studies with Roundup showed very low absorption. Experimental evidence has shown that neither glyphosate nor AMPA bioaccumulates in any animal tissue. No significant toxicity occurred in acute, subchronic, and chronic studies. Direct ocular exposure to the concentrated Roundup formulation can result in transient irritation, while normal spray dilutions cause, at most, only minimal effects. The genotoxicity data for glyphosate and Roundup were assessed using a weight-of-evidence approach and standard evaluation criteria. There was no convincing evidence for direct DNA damage in vitro or in vivo, and it was concluded that Roundup and its components do not pose a risk for the production of heritable/somatic mutations in humans. Multiple lifetime feeding studies have failed to demonstrate any tumorigenic potential for glyphosate. Accordingly, it was concluded that glyphosate is noncarcinogenic. Glyphosate, AMPA, and POEA were not teratogenic or developmentally toxic. There were no effects on fertility or reproductive parameters in two multigeneration reproduction studies with glyphosate. Likewise there were no adverse effects in reproductive tissues from animals treated with glyphosate, AMPA, or POEA in chronic and/or subchronic studies. Results from standard studies with these materials also failed to show any effects indicative of endocrine modulation. ***Therefore, it is concluded that the use of Roundup herbicide does not result in adverse effects on development, reproduction, or endocrine systems in humans and other mammals. For purposes of risk assessment, no-observed-adverse-effect levels (NOAELs) were identified for all subchronic, chronic, developmental, and reproduction studies with glyphosate, AMPA, and POEA. Margins-of-exposure for chronic risk were calculated for each compound by dividing the lowest applicable NOAEL by worst-case estimates of chronic exposure. Acute risks were assessed by comparison of oral LD50 values to estimated maximum acute human exposure. It was concluded that, under present and expected conditions of use, Roundup herbicide does not pose a health risk to humans.*** *" (Williams, GM, et al., 2000)*

The Monsanto Backgrounder on Safety Assessment 2005 (Monsanto, 2005b) is based on this authoritative review paper (Williams, GM, et al., 2000), the key findings:

- *Glyphosate is not a carcinogen,*
- *Roundup herbicide, like glyphosate, has a very low acute toxicity, which means very high exposure is required to cause an adverse effect*
- *Under present and expected conditions of use, Roundup herbicide does not pose a health risk to humans.*
- *Glyphosate does not bioaccumulate*
- *Glyphosate does not adversely affect reproduction or development*
- *Children are not at greater risk*
- *There is no evidence for endocrine disruption*
- *There is no synergistic adverse effect*

Other, more recent comprehensive reviews have been published from the research group of Prof. De Sesso, a leading toxicologist from the USA.

Williams Amy Lavin & deSesso John M. (2010)
Genetically-modified soybeans – Critical evaluation of studies addressing potential ultrastructural changes associated with consumption. Toxicological Sciences, also in The Toxicologist, Supplement 2010, pp
http://www.ask-force.org/web/HerbizideTol/WIlliams-DeSesso-GM-Soy-Poster-2010.pdf
AND http://www.ask-force.org/web/HerbizideTol/WIlliams-DeSesso-GM-Soy-Abstract-2010.pdf

Williams Amy Lavin, Watson Rebecca E., & DeSesso John M. (2012)
Developmental and Reproductive Outcomes in Humans and Animals After Glyphosate Exposure: A Critical Analysis. Journal of Toxicology and Environmental Health, Part B, 15, 1, pp 39-96
http://dx.doi.org/10.1080/10937404.2012.632361
AND http://www.ask-force.org/web/HerbizideTol/Williams-DeSesso-Developmental-Glyphosate-2011.pdf

a comprehensive review on glyphosate tolerant cotton:
May, O.L., Culpepper, A.S., Cerny, R.E., Coots, C.B., Corkern, C.B., Cothren, J.T., Croon, K.A., Ferreira, K.L., Hart, J.L., Hayes, R.M., Huber, S.A., Martens, A.B., McCloskey, W.B., Oppenhuizen, M.E., Patterson, M.G., Reynolds, D.B., Shappley, Z.W., Subramani, J., Witten, T.K., York, A.C., & Mullinix, B.G. (2004)
Transgenic cotton with improved resistance to glyphosate herbicide. Crop Science, 44, 1, pp 234-240
http://www.ask-force.org/web/HerbizideTol/May-Transgenic-Cotton-Improved-2004.pdf

2.2. A comparison between conventional herbicides and glyphosate

The *pesticide* reality in Brazil (nobody really interested...), the following "pesticides" were involved in those negative effects:
"The most widely used pesticides were Roundup® (Glyphosate), Karate® Lambda Cyhalothrin), Herbimix® (Atrazine and Simazine) and Priori Xtra® (Azoxystrobin)."

Salvagni, J., Ternus, R.Z., & Fuentefria, A.M. (2011)
Assessment of the genotoxic impact of pesticides on farming communities in the countryside of Santa Catarina State, Brazil. Genetics and Molecular Biology, 34, 1, pp 122-126
http://www.ask-force.org/web/HerbizideTol/Salvagni-Genotoxic-Impact-Pesticides-2011.pdf

Strangely enough Glyphosate is described as pesticide and there is no distinction made between all mentioned pesticide components, no dose-relationship is established which de-validates the study

considerably. Nevertheless, knowing the studies which focus on Glyphosate toxicity it is justified to conclude that the genotoxic effects described can be allocated to the other real pesticides mentioned.

"In conclusion, it was proven through in vivo piscine micronucleus testing, that water from the Lambedor watershed can be considered genotoxic, with emphasis on the degree of genotoxicity from pollution in the area. This implies the possibility of pesticide effluents discharged into the river constituting a disease-hazard to local populations. It is recommended that the river water be analyzed chemically, with a mind to identifying additional classes of toxicants that may also be contributing to genotoxicity in this specific water-shed." (Salvagni, J, et al., 2011).

2.3. Clinical observations of poisoning with Glyphosate in high doses, usually connected to attempted, but often not successful suicides

A case of clear and massive poisoning, but resolved in Hospital with full recovery, but an alarming "story" for fanatic antis: "gee, look how toxic glyphosate is…." Fact is, that the concentration of the "toxic" glyphosate, to reach the status of acute poisoning you need extremely high concentrations of glyphosate.

Sato, C., Kamijo, Y., Yoshimura, K., & Ide, T. (2011)
Aseptic meningitis in association with glyphosate-surfactant herbicide poisoning. Clinical Toxicology, 49, 2, pp 118-120
<Go to ISI>://WOS:000287967700009, request of full text from author, summary below

The facts: A 58-year-old woman ingested approximately 150 mL of GlySH containing 41%% glyphosate and 15%% polyoxyethyleneamine. Investigations of cerebrospinal fluid (CSF) revealed the presence of glyphosate (122.5 mu g/mL), significant elevation of IL-6 (394 mu g/mL), and pleocytosis (32 cells/mu L) with monocyte dominance. She recovered completely after responding to aggressive supportive care in the intensive care unit. All signs and symptoms suggesting meningitis resolved as the concentration of glyphosate in CSF decreased. She was discharged on day 39 of hospital.
Discussion: These findings suggest that the present case involved aseptic meningitis in association with GlySH poisoning. Conclusion: CNS signs and symptoms induced by aseptic meningitis should be considered in cases of glyphosate-surfactant herbicide poisoning. *(Sato, C, et al., 2011)*

Also other recorded and well documented 50 clinical cases demonstrate, that even with high doses self-administered in a clear suicide attempt had rarely mortal consequences, but up to grade 2 and 3 esophagal injuries: (Chang, CY, et al., 1999):

Chang, C. Y., Y. C. Peng, D. Z. Hung, W. H. Hu, D. Y. Yang and T. J. Lin (1999), Clinical impact of upper gastrointestinal tract injuries in glyphosate-surfactant oral intoxication, Human & Experimental Toxicology, 18, 8, pp. 475-478, <Go to ISI>://000082091500001 AND
http://www.ask-force.org/web/HerbizideTol/Chang-Clinical-Impact-Upper-Gastrointestinal-1999.pdf

"1 Fifty patients with glyphosate-surfactant oral ingestion were studied with upper gastrointestinal (UGI) endoscopic grading using Zargar's modified grading system for mucosal corrosive injury.

2 Esophageal injury was seen in 68% of the patients, gastric injury in 72%, and duodenal injury in 16%, There were no grade 3 injuries. The upper gastrointestinal tract injuries caused by glyphosate-surfactant were minor in comparison with those by other strong acids.

3 The WBC count, amount of glyphosate-surfactant ingested, length of hospital stay and the occurrence of serious complications increased markedly in the group which had grade 2 esophageal injuries. Thus, the severity of the esophageal injuries may be a prognostic factor for the patient with glyphosate-surfactant ingestion.

4 The UGI endoscopy may be indicated for grading esophageal injury in patients who have ingested glyphosate-surfactant in amounts greater than 100 mi. physicians should pay more attention to the patients with grade 2 or 3 esophageal injuries to prevent serious complications and to provide aggressive supportive care". (Chang, CY, et al., 1999)

Even more clinical cases (131) were recorded by (Lee, H-L, et al., 2000). In this survey, 8.4% of the patiens died, details below in the summary.

Lee, H.-L., K.-W. Chen, C.-H. Chi, J.-J. Huang and L.-M. Tsai (2000), Clinical Presentations and Prognostic Factors of a Glyphosate — Surfactant Herbicide Intoxication A Review of 131 Cases, 7, pp. 906-910, http://dx.doi.org/10.1111/j.1553-2712.2000.tb02069.x AND http://www.ask-force.org/web/HerbizideTol/Lee-Clinical-Presentation-Glyphosate-Suicide-2000.pdf

"Objective: Suicide attempts with agricultural chemicals are common in southern Taiwan. Among them, glyphosate-surfactant herbicide (GlySH) intoxication has been encountered with increasing frequency. Although a number of reports have described the clinical course and outcomes following ingestion, predictors of serious complications and mortality have not been elucidated. The purpose of this study was to define predictors of serious complications and probable mortality.
Methods: This was a retrospective study of 131 GlySH-intoxicated patients treated at the National Cheng Kung University Hospital from 1988 to 1995. Medical charts were reviewed and clinical and laboratory variables were abstracted, looking for predictors of mortality.
Results:
The most common symptoms included sore throat (79.5%), and nausea with or without vomiting (73.8%). The most common laboratory findings were leukocytosis (68.0%), low serum bicarbonate (48.1%), and acidosis (35.8%). Overall, 11 of 131 patients (8.4%) died; the mean 6 SEM time to death was 2.8 6 0.8 days after presentation. When comparing the clinical and laboratory characteristics among the survivor and fatality groups, significant differences were identified. Respiratory distress, pulmonary edema, respiratory distress necessitating intubation, shock (systolic blood pressure less than 90 mm Hg), altered consciousness, abnormal chest x-ray, renal failure necessitating hemodialysis, larger amount of ingestion (>200 mL), and hyperkalemia were predictors highly associated with poor outcomes and mortality. *Using multiple logistic regression, three predictors were identified, which may predict mortality in severely intoxicated patients. Conclusions: In managing patients who have larger amount of GlySH ingestion, airway protection, early detection of pulmonary edema, and prevention of further pulmonary damage and renal damage appear to be of critical importance."(Lee, H-L, et al., 2000)*

Another case from Sri Lanka (Roberts, DM, et al., 2010), with 600 patients, but less precisely documented, also came up with 7.7 % mortality, but details are lacking:

Roberts, D. M., N. A. Buckley, F. Mohamed, M. Eddleston, D. A. Goldstein, A. Mehrsheikh, M. S. Bleeke and A. H. Dawson (2010), A prospective observational study of the clinical toxicology of glyphosate-containing herbicides in adults with acute self-poisoning, Clinical Toxicology, 48, 2, pp. 129-136, <Go to ISI>://WOS:000275110400006 AND http://www.ask-force.org/web/HerbizideTol/Roberts-Prospective-Observational-Acute-2010.pdf

Context.
The case fatality from acute poisoning with glyphosate-containing herbicides is approximately 7.7% from the available studies but these have major limitations. Large prospective studies of patients with self-poisoning from known formulations who present to primary or secondary hospitals are needed to better describe the outcome from acute poisoning with glyphosate-containing herbicides. Furthermore, the clinical utility of the glyphosate plasma concentration for predicting clinical outcomes and guiding treatment has not been determined. Objective. To describe the clinical outcomes, dose-response, and glyphosate kinetics following self-poisoning with glyphosate-containing herbicides. Methods. This prospective observational case series was conducted in two hospitals in Sri Lanka between 2002 and 2007. We included patients with a history of acute poisoning. Clinical observations were recorded until discharge or death. During a specified time period, we collected admission (n = 216, including five deaths) and serial (n = 26) blood samples in patients. Severity of poisoning was graded using simple clinical criteria.

Results.
Six hundred one patients were identified; the majority ingested a concentrated formulation (36%, w/v glyphosate). Twenty-seven percent were asymptomatic, 63.7% had minor poisoning, and 5.5% of patients had moderate to severe poisoning. There were 19 deaths (case fatality 3.2%) with a median time to death of 20 h. Gastrointestinal symptoms, respiratory distress, hypotension, altered level of consciousness, and oliguria were observed in fatal cases. Death was strongly associated with greater age, larger ingestions, and high plasma glyphosate concentrations on admission (> 734 mu g/mL). The apparent elimination half-life of glyphosate was 3.1 h (95% CI = 2.7-3.6 h). Conclusions. Despite treatment in rural hospitals with limited resources, the mortality was 3.2%, which is lower than that

reported in previous case series. More research is required to define the mechanism of toxicity, better predict the small group at risk of death, and find effective treatments.

A related publication from Gruere about Indian Farmers Suicides, debunking all the tales and myths which make GM crops directly responsible for the sad tradition of Indian farmers suicides:

Gruere, G. & Sengupta, D. (2011)
Bt Cotton and Farmer Suicides in India: An Evidence-based Assessment. Journal of Development Studies, 47, 2, pp 316-337
<Go to ISI>://WOS:000286778300007 AND
http://www.ask-force.org/web/Cotton/gruere-bt-cotton-suicides-2011.pdf

3. Risk-Benefit analysis of Agriculture with Glyphosate-resistant crops

3.1. Benefits of Glyphosate Agriculture

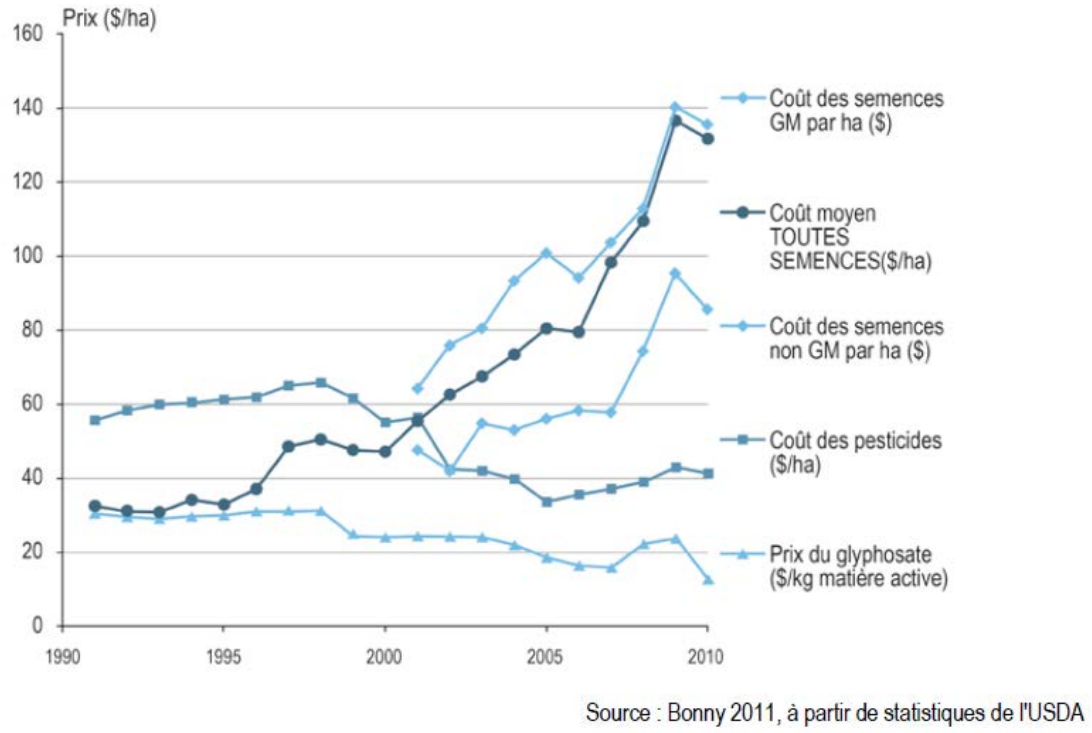

Figure 2 Evolution of seed and pesticide costs for soybeans the USA 1992-2010, after (Bonny, S, 2011), from (Beckert M., YD, C. Charlier, H. Darmency, C. Richard, I. Savini, A. Tibi, 2011)

A case from Canada with clear environmental benefits for HT canola with field data

Smyth, S.J., Gusta, M., Belcher, K., Phillips, P.W.B., & Castle, D. (2011)
Environmental impacts from herbicide tolerant canola production in Western Canada. Agricultural Systems, 104, 5, pp 403-410
http://www.sciencedirect.com/science/article/B6T3W-5259HT0-1/2/12e6902036026591bdbede47ea5fb784 AND
http://www.ask-force.org/web/HerbizideTol/Smyth-Environmental-Impacts-HT-Canola-2011.pdf

"The commercial production of herbicide tolerant (HT) canola began in Western Canada in 1997. With more than a decade of use, the actual farm-level environmental impact of HT canola can be evaluated. This article reports on a spring 2007 survey of nearly 600 canola farmers in the three prairie provinces of Western Canada. Producers were asked about their crop production experiences for 2005 and 2006 and expected crop planting for 2007. A reduction in the total number of chemical applications over the 3-year period was reported, resulting in a decrease of herbicide active ingredient being applied to farmland in Western Canada of nearly 1.3 million kg annually. Fewer tillage passes over the survey period were reported, improving moisture conservation, decreasing soil erosion and contributing to carbon sequestration in annual cropland. An estimated 1 million tonnes of carbon is either sequestered or no longer released under land management facilitated by HT canola production, as compared to 1995. The value of this carbon off-set is estimated to be C$5 million. Comparisons with similar studies and against non-adoption of HT canola can guide future decisions about HT canola adoption" (Smyth, SJ, et al., 2011)

Salvagni, J., Ternus, R.Z., & Fuentefria, A.M. (2011)
Assessment of the genotoxic impact of pesticides on farming communities in the countryside of Santa Catarina State, Brazil. Genetics and Molecular Biology, 34, 1, pp 122-126
http://www.ask-force.org/web/HerbizideTol/Salvagni-Genotoxic-Impact-Pesticides-2011.pdf

The *pesticide* reality in Brazil (nobody really interested...), the following "pesticides" were involved in those negative effects:

"The most widely used pesticides were Roundup® (Glyphosate), Karate® Lambda Cyhalothrin), Herbimix® (Atrazine and Simazine) and Priori Xtra® (Azoxystrobin)."

Strangely enough Glyphosate is described as pesticide and there is no distinction made between all components, no dose-relationship is established which de-validates the study considerably. Nevertheless, knowing the genotoxic studies which focus on Glyphosate it is justified to conclude that the genotoxic effects described can be allocated to the other real pesticides mentioned.

In conclusion, it was proven through *in vivo* piscine micronucleus testing, that water from the Lambedor watershed can be considered genotoxic, with emphasis on the degree of genotoxicity from pollution in the area. This implies the possibility of pesticide effluents discharged into

The whole *scientific* broadside of Monsanto against the glyphosate quackery of the opponents: http://www.monsanto.com/products/Pages/roundup-safety-background-materials.aspx,

More literature on no-till agriculture with Roundup Ready

(Amado, TJC & Reinert, DJ, 1998, Bailey, WA, et al., 2003, Broome, ML, et al., 2000, Brown, SM, et al., 1988, Campiglia, E, et al., 2010, Cerdeira, AL, et al., 2005, Chandler, K, et al., 2001, Corrigan, KA & Harvey, RG, 2000, Davis, VM & Johnson, WG, 2008, Dirks, JT, et al., 2000a, Dirks, JT, et al., 2000b, Foloni, LL, et al., 2001, Ivany, JA, 2004, Lachnicht, SL, et al., 2004, Nelson, KA, et al., 2005, Nunes, AL & Vidal, RA, 2008, Nurse, RE, et al., 2007, Prata, F, et al., 2005, Reddy, KN, 2001, Shirtliffe, SJ & Johnson, EN, 2012, Steckel, LE, et al., 2006, Swanton, CJ, et al., 2000, Tharp, BE & Kells, JJ, 2001, Vangessel, MJ, et al., 2001a, Vangessel, MJ, et al., 2001b, Vanlieshout, LA & Loux, MM, 2000, Wait, JD, et al., 1999, Warnemuende, EA, et al., 2007, Wilson, HP, et al., 1985)

A review on conservation farming in relation to glyphosate use

Towery, D. & Werblov, S. (2010) Facilitating Conservation Farming Practices and Enhancing Environmental, Sustainability with Agricultural Biotechnology Published by the Conservation Technology Information Center, IS: ISBN 978-0-9822440-1-2, pp 1-28
http://www.ctic.purdue.edu/media/pdf/BioTechFINAL%20COPY%20SEND%20TO%20PRINTER.pdf
AND http://www.ask-force.org/web/Soya/Towery-Werblow-Facilitating-Conservation-Farming-2011.pdf

A report from Argentina is pointing to the beneficial effects of crop rotation in glyphosate no-till agriculture related to the development of weeds: (Tuesca, D & Puricelli, E, 2007):

Tuesca, D. and E. Puricelli (2007), Effect of tillage systems and herbicide treatments on weed abundance and diversity in a glyphosate resistant crop rotation, Crop Protection, 26, 12, pp. 1765-1770, <Go to ISI>://000251856600006 AND
http://www.ask-force.org/web/HerbizideTol/Tuesca-Effect-Tillage-Herbicide-Rotation-Argentina-2007.pdf

"The effect of exclusive application of glyphosate and glyphosate in combination with residual herbicides on weed species density and composition in summer crops was studied over 2 years. Field experiments consisted of three rotations including soybean and maize glyphosate-resistant cultivars in two tillage systems. Regardless of the tillage system, both glyphosate application alone and in combination with residual herbicides had a pronounced impact on the reduction in density and richness of summer herbaceous annual weeds, but the effect was greater with glyphosate in combination with residual herbicides."

Finally a well written report by Reinhard Szibor (Szibor Reinhard, 2011) in German, which contains Glyphosate information, in particular the case of a clear TV fraud (ARD 1, first channel) from Germany, see chapter 8.1. where the movie makers claim that a young girl suffers from birth defects

due to glyphosate poisoning. Fact is, that the girl's age excludes that she has been exposed to glyphosate, since she was born some years earlier than the introduction of RR soybeans in her region. When alerted to this embarrassing "mistake", the authors left out the age indication of the girl in the next show….

Scibor, R. (2011)
Memorandum zur Verantwortung der Kirchen hinsichtlich des Themenkreises Grüne Gentechnik Forum Gruene Vernunft www.gruenevernunft.de pp 30 (Report)
http://www.ask-force.org/web/Discourse/Szibor-Memorandum-Kirchen-2011.pdf

A recent debate has been triggered by journalists commenting preliminary, unpublished results of the research team of Ashild Krogdahl in Germany: Unfortunately, peer reviewed publications are not yet available, only a report is published on the latest results of her fish feeding experiments are summarized in the GMSAFOOD report (GMSAFOOD, et al., 2012), the summary – which is not alarming at all:

"NVH reported on a series of feeding trials with Bt maize and its isogenic counterpart conducted on Atlantic salmon. Both healthy fish and fish which were sensitized by dietary inclusion of soybean meal (immune stimulated), were used at various stages of development in studies lasting up to 5 months. The effects of Bt maize on intestinal functions indicateds somewhat less efficient feed utilization and lower body fat deposition. Potentiation of cellular stress in the fish consuming Bt maize and soybean meal was observed, but Bt maize effects did not differ between healthy and sensitized fish. ***No detectable systemic health effects were observed. Antibodies to Cry1Ab protein were not detected. Major health effects were not observed in Atlantic salmon fed with Bt maize but longer term trials may be useful to ensure long term safety****. The results of a transgenerational trial of Zebra fish as a potential model for various fish species was also reported. No adverse effects on growth performance of parents or offspring, nor on reproductive performance of the parents of behviour of offspring in Zebra fish studies were reported. An experiment with AAI peas in the diet for Atlantic salmon showed no change in growth performance." (GMSAFOOD, et al., 2012)*

From a series of publications with co-authorship of Ahild Krogdahl including the abstracts: tere is nothing alarming as well to be derived from the high quality research, the conclusions in the summaries are highlighted in the summaries of the following selection of papers: (Bakke-McKellep, AM, et al., 2008, Cai, C-F, et al., 2012, Cai, C, et al., 2011, Chikwati, EM, et al., 2012, Denstadli, V, et al., 2011, Froystad-Saugen, MK, et al., 2009, Froystad, MK, et al., 2008, GMSAFOOD, et al., 2012, Hansen, JO, et al., 2010, Hansen, JO, et al., 2011, Hemre, GI, et al., 2007, Kortner, TM, et al., 2011, Penn, MH, et al., 2011, Sagstad, A, et al., 2008, Sissener, NH, et al., 2009a, Sissener, NH, et al., 2009b, Sissener, NH, et al., 2011)

Bakke-McKellep, A. M., M. Sanden, A. Danieli, R. Acierno, G. I. Hemre, M. Maffia and A. Krogdahl (2008).
"Atlantic salmon (Salmo salar L.) parr fed genetically modified soybeans and maize: Histological, digestive, metabolic, and immunological investigations." Research in Veterinary Science **84**(3): 395-408.
http://www.ask-force.org/web/HerbizideTol/Bakke-Atlantic-Salmon-Soy-Maize-2007.pdf

Physiological and health related responses to dietary inclusion of genetically modified (GM) full-fat soybean meal (Roundup Ready®; GM-soy) and maize (MON810® Bt-maize; GM-maize), as well as non-parental, untransformed lines (nGM-soy and nGM-maize D2), were evaluated in farmed Atlantic salmon (Salmo salar L.) parr during the first 8 months of feeding. Significant effects of dietary GM presence were only found in intestinal Na+-dependent d-glucose uptake and SGLT1 protein level in the region pyloric caeca in which the highest values were found in the GM-soy, intermediate in the nGM-soy, and lowest in the standard FM fed groups. ***Data from this study confirm that GM soybeans (RRS®) and maize (MON810®) at inclusion levels of about 6% appear to be as safe as commercially available nGM soy and maize in diets for Atlantic salmon parr.*** *Results from studies with higher inclusion levels and with non-modified, isogenic or near-isogenic parental lines as control groups are pending.*

Cai, C., E. Li, Y. Ye, A. Krogdahl, G. Jiang, Y. Wang and L. Chen (2011)
"Effect of dietary graded levels of cottonseed meal and gossypol on growth performance, body composition and health aspects of allogynogenetic silver crucian carp, Carassius auratus gibelio female x Cyprinus carpio male." Aquaculture Nutrition **17**(4): 353-360.

http://www.ask-force.org/web/Feed/Cai-Effect-Cotton-Gossypol-Carp-2011.pdf

A 6-month trial was conducted to evaluate the effects of dietary cottonseed meal (CSM) and free gossypol (FG) on allogynogenetic silver crucian carp, Carassius auratus gibelio female x Cyprinus carpio male with 4 replicates of each treatment. Isonitrogenous and isocaloric diets were formulated with the 0 g kg(-1) (control), 200 g kg(-1), 400 g kg(-1), and 560 g kg(-1) CSM. Diets with FG were made by supplementing batches of control diet with 214 mg kg(-1), 428 mg kg(-1), and 642 mg kg(-1). Weight gain, specific growth rate, and protein efficiency ratio increased significantly up to an inclusion level of CSM of 400 g kg(-1) in the diet, with a significant decrease in food conversion ratio. Further increase in CSM to 560 g kg(-1) did not cause further changes in fish performance. Free gossypol did not affect fish performance significantly at any inclusion level. ***Neither CSM nor FG caused significant effects in any of the other evaluated parameters such as whole body composition, haemoglobin concentration, activities of serum lysozyme, superoxide dismutase, alanine aminotransferase and aspartate aminotransferase, and histology of hepatic tissues and midgut. Our results suggested that crucian carp can tolerate at least 642 mg kg(-1) FG and that it is safe to including 400 g kg(-1) CSM in crucian carp feed****.*

Cai, C.-F., W.-J. Wang, Y.-T. Ye, A. Krogdahl, Y.-L. Wang, Y.-M. Xia and C.-G. Yang (2012).
"Effect of soybean meal, raffinose and stachyose on the growth, body composition, intestinal morphology and intestinal microflora of juvenile allogynogenetic silver crucian carp (Carassius auratus gibelio female x Cyprinus carpio male)." Aquaculture Research **43**(1): 128-138.
http://www.ask-force.org/web/Feed/Cai-Effect-Soybean-Meal-Raffinose-Carp-2012.pdf

The study was conducted to investigate the effects of soybean meal (SBM), raffinose and stachyose on juvenile crucian carp (Carassius auratus gibelio? x Cyprinus carpio?). The experimental diets consisted of one control diet based on fish meal (FM), one diet containing 300 g kg-1 SBM and four FM-based diets with the addition of either 6.7 g kg-1 raffinose (Raf), 33.9 g kg-1 stachyose (Sta), a combination of raffinose and stachyose (Raf-Sta) and finally a Raf-Sta diet supplemented with 2.5 g kg-1 saponins (Raf-Sta-Sap). After 3 weeks of feeding, the relative gut lengths of SBM-fed fish and the fish fed stachyose-containing diets were shorter than those of the FM-fed fish; further, more SBM-fed fish showed fissures on the tips of the intestinal folds. After 8 weeks of feeding, the growth of SBM-fed fish was significantly lower than that of FM-fed fish (P<0.05). The fish fed Raf-Sta-Sap had a low relative gut length (P<0.05). In comparison with the other fish, the SBM-fed fish had a higher number of large-sized homogeneous vacuoles in the cytoplasm of epithelial cells and shorter microvilli. ***No significant difference was observed in body composition or intestinal microflora. The results indicated that raffinose and stachyose played no or only minor roles in the development of soybean-induced growth reduction.***

Chikwati, E. M., F. F. Venold, M. H. Penn, J. Rohloff, S. Refstie, A. Guttvik, M. Hillestad and A. Krogdahl (2012).
"Interaction of soyasaponins with plant ingredients in diets for Atlantic salmon, Salmo salar L." British Journal of Nutrition **107**(11): 1570-1590.
http://www.ask-force.org/web/Feed/Chikwati-Interaction-Soyssabonins-Salmo-2012.pdf

The effects of combining soyasaponins with plant ingredients on intestinal function and fish health were investigated in an 80 d study with Atlantic salmon (270 g) distributed thirty each into twenty-four tanks with seawater. Soyasaponins were supplemented (2 g/kg) to diets with maize gluten (MG), pea protein concentrate (PPC) and sunflower (SFM), rapeseed (RSM) or horsebean meals. A diet with soyabean meal (SBM) and another with wheat gluten and soyasaponins served as reference diets. Marked soyasaponin effects were observed when combined with PPC. This combination induced inflammation in the distal intestine (DI) similar to SBM, reduced feed intake, apparent digestibility of lipid, most amino acids and ash, decreased bile salt levels in intestinal chyme and decreased leucine aminopeptidase (LAP) activity but increased trypsin activity in the DI. No enteritis was observed in other diet groups, but small consistent negative soyasaponin effects were seen on lipid and fatty acid digestibility, faecal DM and LAP activity of the DI. Soyasaponin combination with RSM reduced digestibility of all nutrients including minerals. The mineral effect was also seen for SFM, whereas with MG and SFM a positive soyasaponin effect on feed intake was observed. Caution should be exercised to avoid ingredient combinations giving high saponin levels, a condition that appears to be a key factor in diet-induced enteritis together with certain plant ingredients.

Froystad, M. K., E. Lilleeng, A. M. Bakke-McKellep, K. Vekterud, G. I. Hemre and A. Krogdahl (2008).
"Gene expression in distal intestine of Atlantic salmon (Salmo salar L.) fed genetically modified soybean meal." Aquaculture Nutrition 14(3): 204-214.
http://www.ask-force.org/web/HerbizideTol/Froystad-Gene-Expression-Distal-Intestine-2008.pdf

Limited availability of fishmeal leads to exploration of alternative protein sources like soybean meal (SBM). During the last decade, genetically modified (GM) plants have been introduced to the production of soybean crops. In the current experiment RNA was isolated from the distal intestinal section of Atlantic salmon fed either GM SBM or its near-isogenic parental line (non-GM), both at 30% inclusion. From a suppression subtractive hybridization cDNA library, 95 clones were sequenced. Clones with similarity to both known Atlantic salmon genes and novel Atlantic salmon sequences were identified. Real-time polymerase chain reaction was used to study differential expression of seven clones between the dietary groups. The clones were selected based on their relevance to intestinal immune responses and nutrient metabolism. Expression of a serum lectin-like clone was down-regulated in the GM group compared with the non-

GM group. ***No differential expression was observed for six other clones with similarity to actin-related protein 2/3 complex-subunit 3, cysteine-rich intestinal protein, fatty acid binding protein/gastrotropin, ferritin heavy subunit, anterior gradient protein and peptide transporter. In conclusion, only minor differences in distal intestine transcriptional gene expression were observed between fish fed the diets with the non-GM and GM varieties.***

Penn, M. H., E. A. Bendiksen, P. Campbell and A. Krogdahl (2011).
"High level of dietary pea protein concentrate induces enteropathy in Atlantic salmon (Salmo salar L.)." Aquaculture **310**(3-4): 267-273.
http://www.ask-force.org/web/Feed/Penn-High-Level-Dietary-Pea-2011.pdf

The current study investigated the effects of pea protein concentrate, soy protein concentrate and corn gluten, either singly at high inclusion, or in combination, each at lower inclusion, in diets for Atlantic salmon (Salmo salar L). Growth performance, nutrient digestibility, intestinal brush border enzyme activity, and intestinal histology were studied in an 8-week feeding trial. Triplicate groups of Atlantic salmon (2.36 kg initial weight) were kept in sea water at winter temperature. Five diets were tested, including a control diet based on fish meal (FM diet; 250 g kg(-1) fishmeal) and four low fishmeal (100 g kg(-1)) diets: a diet containing 350 g kg(-1) pea protein concentrate (PPC diet), a diet containing 300 g kg(-1) soy protein concentrate (SPC diet), a diet containing 300 g kg(-1) corn gluten (CG diet) and a combination diet containing 130 g kg(-1) pea protein concentrate, 105 g kg(-1) soy protein concentrate and 105 g kg(-1) corn gluten (CMB diet). Fish fed CG and PPC diets showed lower SGR than fish fed the FM diet and there was a trend (P<0.09) towards a higher feed conversion (FCR) in the fish receiving the CG and PPC diets. Apparent fat digestibility was lower in fish fed SPC. PPC and CMB diets compared to FM. No difference in apparent crude protein digestibility was observed. Feeding the PPC diet resulted in reduced relative weight and inflammation in the distal intestine similar to those described for soy enteritis. Additionally, fish fed the PPC diet had reduced brush border enzyme activities in the distal intestine and increased trypsin activity in the digesta from the distal intestine region. ***In conclusion, pea protein concentrate at high inclusion was shown to induce an enteropathy in the distal intestine of Atlantic salmon and caution should be used when including it in formulated feeds for Atlantic salmon. (C) 2010 Elsevier B.V. All rights reserved.***

Sagstad, A., M. Sanden, A. Krogdahl, A. M. Bakke-McKellep, M. Froystad and G. I. Hemre (2008)).
"Organs development, gene expression and health of Atlantic salmon (Salmo salar L.) fed genetically modified soybeans compared to the near-isogenic non-modified parental line." Aquaculture Nutrition **14**(6).
http://www.ask-force.org/web/HerbizideTol/Sagstad-Organs-Development-Gene-Expression-Health-Soybeans-2008.pdf

The present experiment was conducted to study the possible effects of genetically modified (GM), full-fat soybean meal (FFSBM) from Round-up Ready((R)) soybeans compared to its parental, and closest near-isogenic, non-modified (nGM) soybean variety, added at moderate (150 g kg(-1)) and high (300 g kg(-1)) inclusion levels. The fish showed a high specific growth rate (SGR 1.27-1.52), and nearly doubled their body weight (BW), with final weights varying from 1009 to 1110 g. Increased levels of dietary FFSBM, independent of the soy being GM or not, significantly decreased mean values of SGR, thermal growth rate, condition factor, final BW, liver somatic index, lipid efficiency ratio, apparent digestibility coefficients (ADC) of protein and gross energy, liver lipid content and plasma cholesterol, and significantly increased ADC of starch and muscle fatty acid levels of 18:3n-3, 20:4n-6, 20:5n-3 and total n-3. Increasing dietary GM FFSBM significantly increased feed conversion ratio, and significantly decreased protein efficiency ratio, ADC of lipid and dry matter and plasma triacylglycerol (TAG) levels. Spleen somatic index was significantly larger in fish groups fed GM FFSBM compared to groups fed nGM FFSBM, which might indicate a possible immune response exerted by the GM soybeans. Mean normalized expression of heat shock protein 70 mRNA in distal intestine was significantly up-regulated while normalized expression of catalase in liver was down-regulated, in fish fed FFSBM compared to fish fed FM. ***In conclusion, substituting moderate to high levels of GM Round-up Ready((R)) FFSBM in diets for Atlantic salmon and compared to the closest near-isogenic counterpart available, resulted in many effects independent of the soy being GM or not, but with the notable exceptions of enlarged spleen and lowered plasma TAG.***

Sissener, N. H., A. M. Bakke, J. Gu, M. H. Penn, E. Eie, Å. Krogdahl, M. Sanden and G. I. Hemre (2009)
"An assessment of organ and intestinal histomorphology and cellular stress response in Atlantic salmon (Salmo salar L.) fed genetically modified Roundup Ready® soy." Aquaculture **298**(1-2): 101-110.
http://www.botanischergarten.ch/Feed/Sissener-Assessment-GM-Soy-Salmon-2009.pdf

This study was conducted to investigate potential differences between genetically modified (GM) Roundup Ready® soy and its near-isogenic maternal line as feed ingredients for Atlantic salmon, with focus on intestinal changes commonly caused by soybean meal, histomorphology of other organs and stress response. A 7-month feeding trial was conducted with an inclusion level of 25% GM soy in the diet. Samples for histology were collected after 4 months, after 6 months, when a cross-over of the diet groups was conducted, and at the end of the trial of the crossed-over groups. Histomorphology of spleen, head kidney and mid intestine exhibited no differences between the diet groups, while glycogen deposits in liver were decreased in the GM fed fish at the final sampling. Common soybean meal-induced changes of the distal intestine in Atlantic salmon were observed in both diet groups at all sampling points, within levels expected at the current inclusion level of soy in the diets. However, mucosal fold height in the distal intestine was lower in the GM fed group at one of the three sampling points, and mucosal fold fusion was more pronounced in this group overall in the trial. A stress test conducted at the end of

*the trial gave responses in haematological parameters, plasma nutrients and mRNA transcription of heat shock protein (HSP) 27 in both liver and distal intestine, but responses were similar between the two diet groups, indicating similar ability to handle stress. The cross-over design, implemented to look at reversibility of potential GM-effects, proved to be inadequate as the crossing of diet groups in itself caused responses that would obscure possible minor diet effects**. In conclusion, minor differences were observed between the diet groups; however, GM soy did not appear to cause any adverse effects on organ morphology or stress response compared to non-GM soy.***

Sissener, N. H., M. Sanden, A. M. Bakke, Å. Krogdahl and G. I. Hemre (2009).
"A long term trial with Atlantic salmon (Salmo salar L.) fed genetically modified soy; focusing general health and performance before, during and after the parr-smolt transformation." Aquaculture **294**(1-2): 108-117.
http://www.botanischergarten.ch/Feed/Sissener-Long-Term-Trial-GM-Soy-Salmo-2009.pdf

*A seven-month feeding trial with genetically modified (GM) Roundup Ready® (RRS®) soybeans was conducted on Atlantic salmon (initial weight 40 g) going through the parr-smolt transformation. The maternal near-isogenic soybean line was used as a non-modified control (non-GM), and the two diets were compositionally similar in all analysed nutrients. The performance and health of the fish were assessed by growth, body composition, organ development, haematological parameters, clinical plasma chemistry and lysozyme levels, with samples collected both in the freshwater- and seawater stages. Intestinal indices exhibited some differences between the groups, with the mid-intestine being consistently smaller in the GM fed fish throughout the experiment, while the distal intestine was different at one sampling point, shortly after seawater transfer. Plasma triacylglycerol (TAG) levels were higher in the GM group overall in the experiment, although the magnitude of the difference was larger around the time of seawater transfer compared to later samplings. Despite differences at individual sampling points, there were no differences in total growth during the trial. All other measured parameters showed no diet related differences. Seawater transfer caused changes in gill Na+K+-ATPase activity and plasma chloride ion concentration, as well as in haematological parameters (red blood cell count, RBC, haematocrit, Hct, haemoglobin, Hb) and plasma glucose concentration. However, both diet groups responded similarly regarding these parameters. **Our overall conclusion is that the observed effects of feeding Atlantic salmon with GM soy at a 25% inclusion level were minor, and lack of consistency with previous studies suggests that they might be caused by variations in the soy strains rather than the genetic modification per se.***

Sissener, N. H., M. Sanden, A. Krogdahl, A.-M. Bakke, L. E. Johannessen and G.-I. Hemre (2011)
"Genetically modified plants as fish feed ingredients." Canadian Journal of Fisheries and Aquatic Sciences **68**(3): 563-574.
http://www.ask-force.org/web/Feed/Sissener-GM-plnts-Fish-Feed-2011.pdf

Genetically modified (GM) plants were first grown commercially more than 20 years ago, but their use is still controversial in some parts of the world. Many GM plant varieties are produced in large quantities globally and are approved for use in fish feeds both in Norway and the European Union. European consumers, however, are skeptical to fish produced by means of GM feed ingredients. Concerns have been raised regarding the safety of GM plants, including potential toxicity and (or) allergenicity of the novel protein, potential unintended effects, and risk of horizontal gene transfer to other species. This review will present the current state of knowledge regarding GM plants as fish feed ingredients, focusing on fish performance and health as well as the fate of the GM DNA fragments in the fish, identifying limitations of the current work and areas where further research is needed.

Gatlin, D. M., III, F. T. Barrows, P. Brown, K. Dabrowski, T. G. Gaylord, R. W. Hardy, E. Herman, G. Hu, A. Krogdahl, R. Nelson, K. Overturf, M. Rust, W. Sealey, D. Skonberg, E. J. Souza, D. Stone, R. Wilson and E. Wurtele (2007).
"Expanding the utilization of sustainable plant products in aquafeeds: a review." Aquaculture Research **38**(6): 551-579.
http://www.ask-force.org/web/HerbizideTol/Gatlin-Expanding-Utilization-Sustainable-Plant-Products-2007.pdf

*Continued growth and intensification of aquaculture production depends upon the development of sustainable protein sources to replace fish meal in aquafeeds. This document reviews various plant feedstuffs, which currently are or potentially may be incorporated into aquafeeds to support the sustainable production of various fish species in aquaculture. The plant feedstuffs considered include oilseeds, legumes and cereal grains, which traditionally have been used as protein or energy concentrates as well as novel products developed through various processing technologies. The nutritional composition of these various feedstuffs are considered along with the presence of any bioactive compounds that may positively or negatively affect the target organism. **Lipid composition of these feedstuffs is not specifically considered although it is recognized that incorporating lipid supplements in aquafeeds to achieve proper fatty acid profiles to meet the metabolic requirements of fish and maximize human health benefits are important aspects. Specific strategies and techniques to optimize the nutritional composition of plant feedstuffs and limit potentially adverse effects of bioactive compounds are also described**. Such information will provide a foundation for developing strategic research plans for increasing the use of plant feedstuffs in aquaculture to reduce dependence of animal feedstuffs and thereby enhance the sustainability of aquaculture.*

Hemre, G. I., A. Sagstad, A. M. Bakke-Mckellep, A. Danieli, R. Acierno, M. Maffia, M. Froystad, A. Krogdahl and M. Sanden (2007)
"Suitability of genetically modified soybean meal in rainbow trout diets." Aquaculture Nutrition **13**(3): 186-199.
http://www.botanischergarten.ch/Feed/Hemre-Nutritional-Physiological-GM-Maize-Salmo-2007.pdf

The objective of this study was to evaluate whether standard fish meal diets prepared with increasing levels of genetically modified (GM; 150 and 300 g kg(-1)) maize (event MON810((R))) as a starch source, showed any nutritional or physiological adverse effects on Atlantic salmon, Salmo salar L. postsmolt. The diets with low or high inclusions of GM maize and its near-isogenic parental line (nongenetically modified; nGM maize), were balanced with Suprex maize (Reference) to obtain compositional equivalency of diet starch, sugars and all other nutrients. Total starch level in all diets was 160 g kg(-1). After 82 days of feeding, fish growth was high in all groups, however fish fed the GM maize showed slight but significant lower feed intake, which was followed by slight but significant lower specific growth rate and final body weights, compared with fish fed nGM maize, none of the groups varied significantly from fish fed the Reference diet. There was no variation in feed conversion ratios (FCR), protein and lipid efficiency ratios (PER and LER), or protein- and lipid-productive values (PPV and LPV) in this study. No significant effect of maize type was detected on apparent digestibility coefficients (ADC) of dry matter, protein or lipid. Hematological analysis and plasma nutrients varied within normal ranges for Atlantic salmon in all diet groups, except for somewhat elevated aspartate aminotransferase (ASAT) values in all groups. Hepatosomatic index (HSI) with values ranging from 1.37 to 1.60, was significantly higher for the high GM maize group compared with the high nGM maize group but not when compared with the Reference diet group. Lowered spleen (SSI) and head-kidney somatic indices (H-KSI) were registered when fed GM compared with nGM maize, the Reference treatment was however, equal to both. Distal intestine somatic index (DISI) was significantly higher for GM maize-fed fish compared with nGM maize-fed fish, but not significantly different from the Reference diet group. Histological evaluation of the mid- and distal intestine, liver, spleen and head-kidney did not reveal any diet-related morphological changes. Maltase activities in the mid- and distal intestinal tissue homogenates were affected by diet, the fish fed high GM maize having higher activities compared with high nGM maize-fed fish. Leucine aminopeptidase (LAP) and alkaline phosphatase (AP) activities were not affected by diet. Sodium-dependent D-glucose uptake in brush border membrane vesicles (BBMV) isolated from pyloric caeca of fish fed high GM maize was significantly higher than that found in fish fed the analogous diet with high nGM maize. ***Based on the present findings, the conclusions made are: Atlantic salmon smolts fed GM maize (event MON810((R))), its near-isogenic parental line and suprex maize (Reference diet), all resulted in high growth rates, ADC and feed utilization. Health, when evaluated by means of mortality (low), normal ranges of blood and plasma parameters, except somewhat elevated ASAT values and minor variations in organ sizes, were considered good in all diet groups. The changes in the glucose transport mechanism and intestinal maltase enzyme activity in the gastrointestinal tract warrant further studies.***

Nevertheless, journalists are again playing the loudspeakers of anti-GMO-people without critical scrutiny of the results of the Norwegian research group,

3.2. The Weed Problem of Glyphosate Agriculture

In the first few years of Glyphosate introduction in combination with herbicide tolerant crops there was optimism, that the very special locus of the EFPS-gene causing tolerance would not be achieved in short time by weeds and their frequent mutations, but this revealed to be not correct. Although the development of glyphosate resistant weeds does by far not reach the size of other herbicides, it is beginning to be an agricultural problem, but there are data and realistic views that the problems can be handled:

Wilson, R. G., B. G. Young, J. L. Matthews, S. C. Weller, W. G. Johnson, D. L. Jordan, M. D. K. Owen, P. M. Dixon and D. R. Shaw (2011), Benchmark study on glyphosate-resistant cropping systems in the United States. Part 4: Weed management practices and effects on weed populations and soil seedbanks, Pest Management Science, 67, 7, pp. 771-780, <Go to ISI>://WOS:000292411800004 AND http://www.ask-force.org/web/HerbizideTol/Wilson-Benchmark-Study-Glyphosate-Resistant-Weeds-US-2011.pdf

"The abstract and conclusions:
BACKGROUND: Weed management in glyphosate-resistant (GR) maize, cotton and soybean in the United States relies almost exclusively on glyphosate, which raises criticism for facilitating shifts in weed populations. In 2006, the benchmark study, a field-scale investigation, was initiated in three different GR cropping systems to characterize academic recommendations for weed management and to determine the level to which these recommendations would reduce weed population shifts.

RESULTS: Amajority of growers used glyphosate as the only herbicide for weed management, as opposed to98% of the academic recommendations implementing at least two herbicide active ingredients and modes of action. The additional herbicides were applied with glyphosate and as soil residual treatments. The greater herbicide diversity with academic recommendations reduced weed population densities before and after post-emergence herbicide applications in 2006 and 2007, particularly in continuous GR crops.

CONCLUSION: Diversifying herbicides reduces weed population densities and lowers the risk of weed population shifts and the associated potential for the evolution of glyphosate-resistant weeds in continuous GR crops. Altered weed management practices (e.g. herbicides or tillage) enabled by rotating crops, whether GR or non-GR, improves weed management and thus
minimizes the effectiveness of only using chemical tactics to mitigate weed population shifts".

The situation is not as dramatic yet, compared to other herbicides, shown by the most recent graph of “Weed Science” website: (Weed Science, 2012)

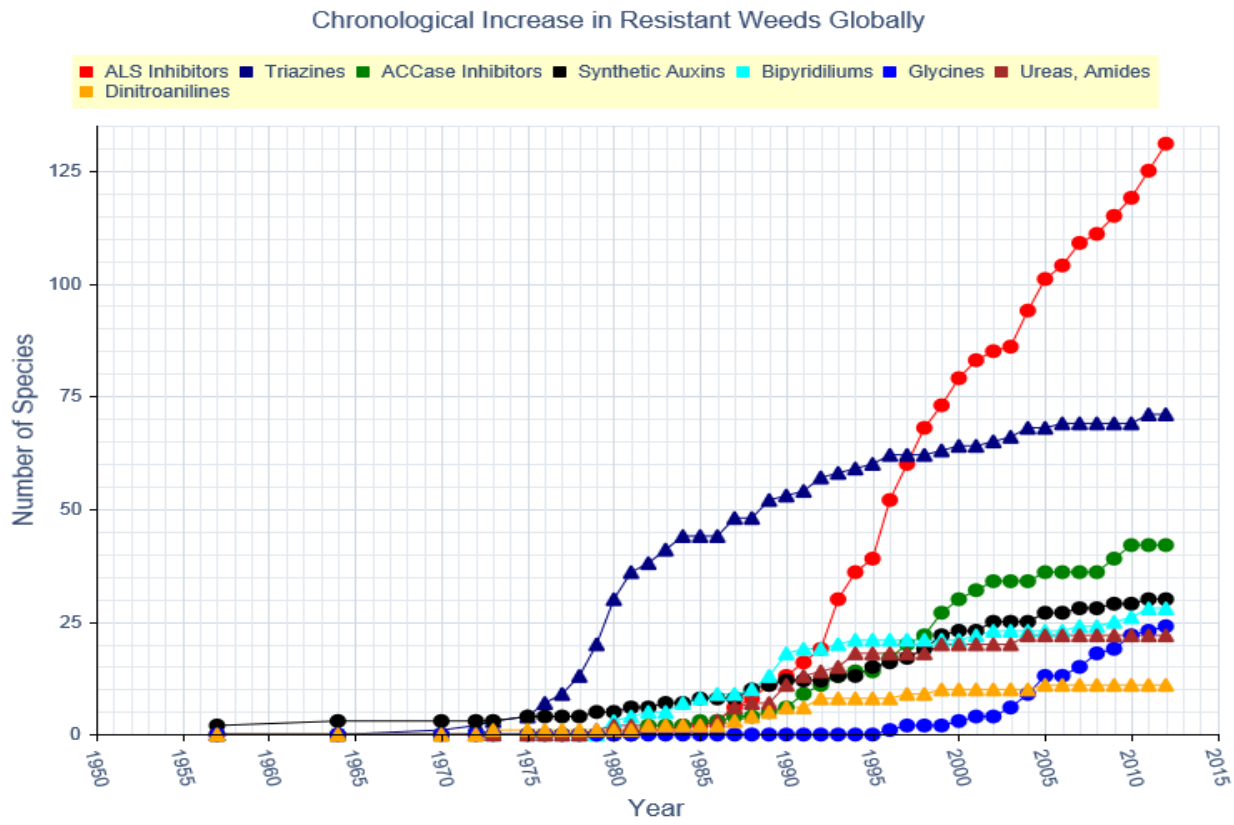

Figure 3 ©2013 WeedScience.org, Dr. Ian Heap 06/24/2013 http://www.weedscience.org/Graphs/SOAGraph.aspx

There are much more references to discuss:

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The above literature selection with annotations and comments, cited below, is a short extract of a bibliography of 5028 references (20130915) on herbicide tolerant crops collected over many years by Klaus Ammann, the main source: Web of Science.

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