Backgrounder
Response to "Glyphosate Toxic & Roundup Worse"
Updated April 2006

On March 7, 2005, The Institute of Science in Society (London, England) published an editorial by Dr. Mae-Wan Ho and Prof. Joe Cummins (see Appendix). This editorial called for urgent regulatory review of the most widely used herbicide in the light of new scientific evidence.

Ho and Cummins make the following statements:

- *"New research findings are raising serious concerns over the safety of the most commonly used herbicide, and should be sending shock waves through proponents of genetically modified (GM) crops made tolerant to the herbicide, which now account for 75% of all GM crops in the world.*"
- *"There is now a wealth of evidence that glyphosate requires worldwide health warnings and new regulatory review. Meanwhile, its use should be reduced to a minimum as a matter of prudent precaution."*

This document provides **direct responses** to six points that Ho and Cummins cite as evidence supporting a worldwide health warning, regulatory review and reduction in use of glyphosate and Roundup branded agricultural herbicides.

Point 1. "*However, glyphosate acts by preventing the binding of phosphoenol pyruvate to the active site of the enzyme, and phosphoenol pyruvate is a core metabolite present in all organisms; thus it has the potential to affect other metabolic pathways. This is borne out by many reports of toxicities associated with the herbicide reviewed in the Independent Science Panel Report, The Case for a GM-Free Sustainable World* ."[1]

Response:

- While the Independent Science Panel (ISP) could be considered "independent" as it is not formally affiliated with other organizations or institutions, the ISP members are opponents of plant biotechnology and have a long-standing position in opposition to this technology (see http://www.i-sis.org.uk/ispr-summary.php).

  While it is true that phosphoenol pyruvate is an important compound in the metabolism of virtually all plant and animal species, no effect of glyphosate on pyruvate metabolism in mammalian cells has ever been demonstrated. Glyphosate targets an enzyme not present in animal species and is not known to influence pyruvate metabolism by any other mechanism which would be relevant to humans or animals.

[1] The Case for a GM-Free Sustainable World, Chapter 7, ISIS & TWN, London & Penang, 2003. http://www.indsp.org/A GM-Free Sustainable World.pdf

Credible evaluations of Roundup branded agricultural herbicides and the active ingredient glyphosate can be obtained from the following:

- EPA Reregistration Eligibility Decision: Glyphosate (September 1993):
  Fact Sheet: http://www.epa.gov/oppsrrd1/REDs/factsheets/0178fact.pdf
  Full RED: http://www.epa.gov/oppsrrd1/REDs/old_reds/glyphosate.pdf
- European Commission (2002) Report for the Active Substance Glyphosate, Directive 6511/VI/99, January 21.
  http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1_glyphosate_en.pdf
- WHO Environmental Health Criteria 159: Glyphosate (1994):
  http://www.inchem.org/documents/ehc/ehc/ehc159.htm
- Pesticide Residues in Food (2004). Report of the Joint FAO/WHO Meeting of Experts
  http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/DOWNLOAD/2004_rep/report2004jmpr.pdf

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Point 2. *"An epidemiological study in the Ontario farming populations showed that glyphosate exposure nearly doubled the risk of late spontaneous abortions.* [2] *"*

Response:

- **Glyphosate does not cause miscarriages.**

Glyphosate is one of many pesticides mentioned in an epidemiological report that examined possible links between self-reported, on-farm pesticide use and self-reported reproductive outcomes. Savitz *et al.* (1997) used data from the Ontario Farm Family Health Study (OFFHS) and investigated associations between reported pesticide use by males and pregnancy outcomes, specifically: miscarriage, pre-term delivery and small-for-gestational-age birth. Savitz *et al.* found that a number of specific pesticides had weak statistical associations with miscarriages and pre-term deliveries, but pesticides tended not to be associated with small for gestational age births. There were no statistically significant findings for glyphosate.

Epidemiology studies of this type differ from biomonitoring studies in that groups of people – some with illnesses and some without – are asked to recall what pesticides they may have used or come in contact with. Those studies depend on the ability of the person to recall accurately, but more importantly, they do not measure whether there actually was any internal exposure or the extent of such exposure.

There was no quantified exposure data in this epidemiologic study by Savitz *et al*. Exposures were assumed based on questionnaire responses by study subjects about farm activities and pesticide use. This type of information can be inaccurate. Exposure related to the professional use of glyphosate-based formulations, through the monitoring of the single active ingredient glyphosate, has been the subject of a number of studies. The most recent published study is that by Acquavella *et al*.(2004).

[2] Savitz DA, Arbuckle, Kaczor D, Curtis KM. (2000) Male pesticide exposure and pregnancy outcome. *Am J Epidemiol* 146: 1025-36.

Aquavella *et al.* (2004) found that only sixty percent of the farmers were found to have detectable levels of glyphosate in their urine on the day of application and that the geometric mean concentration was 3.2 ppb. The limit of detection was 1 ppb. The distribution of detectable values was highly skewed to low exposure since most detectable values were close to the limit of detection; the highest observed concentration was 233 ppb. Based on estimates of systemic dose, a farmer who did 10 applications per year for 40 years with this highest level of exposure would receive an exposure approximately 31,938 fold below a lifetime systemic dose that corresponds to the US Environmental Protection Agencies reference dose (equivalent to the ADI) of 2 mg/kg/day.

The results of the Savitz *et al.* study do not meet generally accepted criteria from the epidemiology literature for determining causal relationships. First, the associations were very weak and not statistically significant. Secondly, control for potential confounding factors, including other pesticides, was not possible due to limited available information and small numbers of subjects. Thirdly, there was no indication in these studies of a dose-response relationship. Lastly, there was no biological plausibility, the experimental evidence from several studies with laboratory animals show that glyphosate is not a reproductive or developmental toxicant. (EU 2002; EPA 1993; Williams *et al.* 2000).

Therefore, based on the extremely low exposures expected for humans, the lack of biological plausibility, and the lack of statistical significance, the reported association of adverse health effects in epidemiologic studies are unlikely to be valid.

Response References

Acquavella JF, Doe J, Tomenson J, Chester G, Cowell J, Bloemen L. 2003. Epidemiologic Studies of Occupational Pesticide Exposure and Cancer: Regulatory Risk Assessments and Biologic Plausibility. Annals of Epidemiology 13: 1-7.

Acquavella JF, Alexander BH, Mandel JS, Gustin C, Baker B, Chapman P, Bleeke M. 2004. Glyphosate Biomonitoring for Farmer-Applicators and their Families: Results from the Farm Family Exposure Study. Environ Health Perspect 112:321-326.

EPA Reregistration Eligibility Decision: Glyphosate (September 1993):
Fact Sheet: http://www.epa.gov/oppsrrd1/REDs/factsheets/0178fact.pdf
Full RED: http://www.epa.gov/oppsrrd1/REDs/old_reds/glyphosate.pdf

European Commission. 2002. Report for the Active Substance Glyphosate, Directive 6511/VI/99, January 21.
http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1_glyphosate_en.pdf

Williams GM, Kroes R, Munro IC. 2000. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regul Toxicol Pharmacol 31: 117-165. http://dx.doi.org/10.1006/rtph.1999.1371

Point 3. *"Prof. Eric-Giles Seralini and his research team from Caen University in France decided to find out more about the effects of the herbicide on cells from the human placenta. They have now shown that glyphosate is toxic to human placental cells, killing a large proportion of them after 18 hr of exposure at concentrations below that in agricultural use.* [3]*"*

Response:

- **This study by Richard *et al.* tells us nothing about real-world risks to humans. Instead, it tells us what we already know – substances can injure unprotected cells in a test-tube. In the real world, Roundup agricultural herbicides have been used safely by farm workers for more than 30 years. The conclusions of the authors are contradicted by extensive animal studies and by extensive human experience.**

  The following response document is available:

  > **Glyphosate: Response to "Differential effects of glyphosate and Roundup on human placental cells and aromatase"**
  > (http://www.monsanto.com/products/Documents/glyphosate-background-materials/Bkg_Richard_Response_2005.pdf)

  Some of the financial support for this research came from CRII-GEN. Professor Seralini is a member of this anti-biotech organization. (http://www.crii-gen.org/)

  It is also of interest to note that one of the first public forums that Professor Seralini discussed this research was during an interview with The Pesticide Action Network (PAN). (http://www.pan-uk.org/pestnews/Issue/pn63/pn63p4.htm)

  PAN is an inappropriate reference source to use for credible scientific and/or medical information on glyphosate. PAN is a global network of over 600 participating nongovernmental organizations, institutions and individuals in over 60 countries working to replace the use of what they perceive as hazardous pesticides. PAN, at its Fifth International Conference in Dakar, Senegal on May 21, 2000, stated in "The Dakar Declaration": "We commit ourselves to fight for the elimination of pesticides, the termination of genetic engineering of organisms in food and agriculture, the end of corporate globalization and the realization of food sovereignty and sustainable agriculture worldwide" (http://www.pan-international.org/pan-v1/dakarDeclarationEn.html). The lead author of the glyphosate summary referenced by the authors is Meriel Watts. She is spokesperson for the Pesticide Action Network, Aotearoa, New Zealand.

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[3] Richard S, Moslemi S, Sipahutar H, Benachour N and Seralini G-E. (2005) Differential effects of glyphosate and Roundup on human placental cells and aromatases. *Environmental Health Perspectives*, in press. http://dx.doi.org/doi:10.1289/ehp.7728

Point 4. *"There is, indeed, direct evidence that glyphosate inhibits RNA transcription in animals at a concentration well below the level that is recommended for commercial spray application Transcription was inhibited and embryonic development delayed in sea urchins following exposure to low levels of the herbicide and/or the surfactant polyoxyethyleneamine. The pesticide should be considered a health concern by inhalation during spraying.[4] "*

Response:

- **This study by Marc *et al.* tells us nothing about real-world risks to humans. Instead, it tells us what we already know – substances can injure unprotected cells in a test-tube. In the real world, Roundup agricultural herbicides have been used safely by farm workers for more than 30 years. The conclusions of the authors are contradicted by extensive animal studies and by extensive human experience.**

  Marc and her colleagues conducted *in vitro* studies using sea urchins. They have now published a number of articles based on the faulty premise that Roundup is enhancing the ability of glyphosate to get into cells to disrupt the cell cycle. While they measure a variety of cellular/molecular endpoints in these studies, the results are not reflective of cellular effects in real-life systems since non-specific changes in cell membrane function have been shown to occur due to surfactants and may also result from other changes in the culture medium such as effects on pH and calcium levels Note that when the sea urchin embryos are placed back in normal medium they develop into normal sea urchins, indicating a lack of any permanent biological effect.

  When surfactants found in products such as bath gels and shampoos that humans put directly on their bodies everyday were tested in the sea urchin assay they produced the same results as Marc *et al.* did ...cell cycle delays; see http://www.ncbi.nlm.nih.gov/pubmed/9828259?dopt=Abstract).

  Other researchers have found that caffeine also alters cell division in sea urchin embryos (see http://www.ncbi.nlm.nih.gov/pubmed/9276510?dopt=Abstract).

  One could focus on these findings and claim a variety of threats to human safety from shampoo, coffee, tea, and chocolate. A more scientifically appropriate conclusion, knowing what we do about the safety of these consumer products, is that the sea-urchin test system is simply not relevant to predicting adverse effects on human health.

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[4] Marc J, Le Breton M, Cormier P, Morales J, Belle R, Mulner-Lorillo O. (2005) A glyphosate-based pesticide impinges on transcription. *Toxicology and Applied Pharmacology* 203: 1-8.

Point 5. *"New research shows that a brief exposure to commercial glyphosate caused liver damage in rats, as indicated by the leakage of intracellular liver enzymes. In this study, glyphosate and its surfactant in Roundup were also found to act in synergy to increase damage to the liver.* [5] *"*

Response:

- **No similar effects on the liver were found in rats tested at high doses in regulatory studies conducted according to international guidelines under Good Laboratory Practices. (EU 2002, EPA 1993 and Williams et al 2000)**

  Due to the poor conduct and reporting of this study as well as the lack of corroborative findings in studies conducted according to international guidelines under Good Laboratory Practices the findings and conclusions of these authors are not credible.

  A critical flaw is the authors never tested glyphosate alone they only tested dilutions of a glyphosate-based formulation even though they report "We showed that glyphosate and its formulation products may act in synergy on the liver metabolism and/or injury."

  In order to evaluate combined effects it is necessary to determine the response of each agent alone; synergism is noted if the combination of the two agents produces a response that exceeds the sum of the two responses. The only substance tested was the formulation and since the formulation already contains glyphosate the comparison does not hold true. The study design should have been with two groups to be tested; glyphosate alone and the formulation-minus glyphosate.

Response References

EPA Reregistration Eligibility Decision: Glyphosate (September 1993):
Fact Sheet: http://www.epa.gov/oppsrrd1/REDs/factsheets/0178fact.pdf
Full RED: http://www.epa.gov/oppsrrd1/REDs/old_reds/glyphosate.pdf

European Commission (2002) Report for the Active Substance Glyphosate, Directive 6511/VI/99, January 21.
http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1_glyphosate_en.pdf

Williams GM, Kroes R, Munro IC. 2000. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regul Toxicol Pharmacol 31:117-165. http://dx.doi.org/10.1006/rtph.1999.1371

[5] Benedetti AL, de Lourdes Vituri C, Trentin AG, Domingues MAC, Alvarez-Silva M. (2004) The effects of sub-chronic exposure of Wistar rats to the herbicide Glyphosate-Biocarb. *Toxicology Letters* 153: 227-232. http://dx.doi.org/10.1016/j.toxlet.2004.04.008

Point 6. *"Three recent case-control studies suggested an association between glyphosate use and the risk of non-Hodgkin lymphoma [6,7,8] while a prospective cohort study in Iowa and North Carolina that includes more than 54 315 private and commercial licensed pesticide applicators suggested a link between glyphosate use and multiple myoeloma [9]. Myeloma has been associated with agents that cause either DNA damage or immune suppression. These studies did not distinguish between Roundup and glyphosate, and it would be important for that to be done."*

Response:

- **Glyphosate is not carcinogenic or mutagenic. In June 1991, the US EPA placed glyphosate in the agency's most positive cancer classification (Category E) "evidence of non-carcinogenicity for humans--based on the lack of convincing evidence of carcinogenicity in adequate studies." There is no credible evidence that glyphosate or that Roundup herbicides cause cancer in humans.**

  Regulatory authorities and independent experts around the world agree that glyphosate, the active ingredient in Roundup brand agricultural herbicides, does not cause cancer, even at very high doses.

  The World Health Organization, in its 1994 review of glyphosate studies, states: "Animal studies show that glyphosate is not carcinogenic."

  The U.S. Environmental Protection Agency (EPA), after reviewing studies conducted for re-registration of glyphosate, stated in 1993: "Several chronic toxicity/carcinogenicity studies…resulted in no effects based on the parameters examined, or resulted in findings that glyphosate was not carcinogenic in the study." EPA rates all pesticides according to their potential to cause cancer. In June 1991, EPA placed glyphosate in the agency's most positive cancer classification (Category E) "evidence of non-carcinogenicity for humans--based on the lack of convincing evidence of carcinogenicity in adequate studies."

  The most recent review was conducted by the European Commission's Health and Consumer Protection Directorate-General, after which glyphosate was re-registered for use in Europe (Jan. 21, 2002). The EC review, like others around the world, concluded that glyphosate is not carcinogenic. Reviews in Canada and Japan also found no evidence of cancer in glyphosate studies as well three independent scientists (Williams *et al.,* 2000)

  It is important to note that, in the most recent study by DeRoos *et al.* (2005), cancer rates were found to be the same for glyphosate users and non-users. Furthermore, no association was found between glyphosate users and all major types of cancers including the lymphopoetic cancers – non-Hodgkin's lymphoma (NHL), leukemia and multiple myeloma. Only in one analysis of a restricted subgroup of the study population, there was a weak association between frequency of glyphosate use and multiple myeloma. However, other

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[6] De Roos AH, Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, Burmeister LF, Blair A. (2003) Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occup Environ Med* 60: E11.

[7] Hardell L, Eriksson M, Nordstrom M. (2002) Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: Pooled analysis of two Swedish case-control studies. *Leuk Lymphoma* 43: 1043-1049.

[8] McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, Dosman JA, Robson D, Skinnider LF, Choi NW. (2001) Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health. *Cancer Epidemiol Biomarkers Prev* 10:1155-1163.

[9] De Roos AJ, Blair A, Rusiecki JA, Hoppin JA, Svec M, Dosemeci M, Sandler DP and Alavanja MC. (2005) Cancer incidence among glyphosate-exposed pesticide applicators in the agricultural health study. *Environ Health Perspect* 113: 49-54.

analyses in the paper were conflicting in this matter. In any large study with hundreds of statistical analyses, occasional weak associations are expected by chance alone.

Regarding NHL, conflicting results have reported by De Roos *et al.* In 2003, De Roos *et al.* reported that there was an association with glyphosate and NHL. In 2005, De Roos *et al.* reported no association between glyphosate and NHL. Furthermore, it is important to point out that the De Roos *et al.* (2003) paper was a re-analysis of data from three studies in the 1980's, in which no association for glyphosate with NHL was observed.

The four references above are all epidemiologic studies. Epidemiology studies differ from biomonitoring studies in that groups of people – some with illnesses and some without – are asked to recall what pesticides they may have used or come in contact with. Those studies depend on the ability of the person to recall accurately, but more importantly, they do not measure whether there actually was any internal exposure or the extent of such exposure.

There was no measured exposure data in these epidemiologic studies by De Roos *et al.*, Hardell *et al.* and McDuffie *et al.*. Exposures were assumed based on questionnaire responses by study subjects about farm activities and pesticide use. This type of information can be inaccurate. Exposure related to the professional use of glyphosate-based formulations, through the monitoring of the single active ingredient glyphosate, has been the subject of a number of studies. The most recent published study is that by Acquavella *et al*.(2004).

When evaluating epidemiologic findings, it can be helpful to compare the range of likely exposure levels to the exposure levels of toxicologic significance (Acquavella *et al.* 2003). The cancer no-effect levels for glyphosate, based on rat and mouse lifetime feeding studies, are 1,000 and 1,500 mg/kg/day, respectively (Williams *et al.* 2000). Acquavella *et al.* (2004) reported results of a biomonitoring study in which 48 farmers collected all of their urine over 5 consecutive days (before, during, and for 3 days after a glyphosate application). In this study, the maximum systemic dose resulting from application of glyphosate to areas as large as 400 acres was 0.004 mg/kg. The geometric mean systemic dose was 0.0001 mg/kg. Accordingly, in the worst-case situation, had a farmer made a similar application every day for a lifetime, the systemic dose would be at least 250,000-fold lower than the cancer no-effect level in rodents. Indeed, this very large margin of exposure combined with the lack of evidence for genotoxicity must be factored into an assessment of biological plausibility.

Based on the consistent finding that glyphosate is not carcinogenic or mutagenic, the conflicting associations of glyphosate with NHL and multiple myeloma, and the extremely low exposures expected for humans, the reported association of adverse health effects in epidemiologic studies is unlikely to be valid.

Response References:

Acquavella JF, Doe J, Tomenson J, Chester G, Cowell J, Bloemen L. 2003. Epidemiologic Studies of Occupational Pesticide Exposure and Cancer: Regulatory Risk Assessments and Biologic Plausibility. Annals of Epidemiology 13: 1-7.

Acquavella JF, Alexander BH, Mandel JS, Gustin C, Baker B, Chapman P, Bleeke M. 2004. Glyphosate Biomonitoring for Farmer-Applicators and their Families: Results from the Farm Family Exposure Study. Environ Health Perspect 112:321-326.

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WHO. 1994. Glyphosate. Environmental Health Criteria 159. International Programme on Chemical Safety. World Health Organization. Geneva, Switzerland. http://www.inchem.org/documents/ehc/ehc/ehc159.htm

Williams GM, Kroes R, Munro IC. 2000. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regul Toxicol Pharmacol 31: 117-165. http://dx.doi.org/10.1006/rtph.1999.1371

Appendix

Following is the item that this response document is addressing:

From **Institute of Science in Society** website: http://www.i-sis.org.uk/GTARW.php
ISIS Press Release, March 7, 2005

Glyphosate Toxic & Roundup Worse

Dr. Mae-Wan Ho and Prof. Joe Cummins call for urgent regulatory review of the most widely used herbicide in the light of new scientific evidence

New research findings are raising serious concerns over the safety of the most commonly used herbicide, and should be sending shockwaves through proponents of genetically modified (GM) crops made tolerant to the herbicide, which now account for 75% of all GM crops in the world.

Worse yet, the most common formulation of the herbicide is even more toxic than the herbicide by itself, and is made by the same biotech giant that created the herbicide tolerant GM crops.

Broad-spectrum herbicide glyphosate (N-(phosphonomethyl)glycine), commonly sold in the commercial formulation Roundup (Monsanto company, St. Louis, Missouri USA) has been frequently used both on crops and non-crops areas world wide since it was introduced in the 1970s. Roundup is a combination of glyphosate with other chemicals including a surfactant (detergent) polyoxyethyleneamine that enhance the spreading of the spray droplets on the leaves of plants. The use of Roundup has gone up especially in countries growing Roundup-tolerant GM crops created by Monsanto.

Glyphosate kills plants by inhibiting the enzyme, 5-enolpyruvoyl-shikimate-3-phosphate synthetase (EPSPS), essential for the formation of aromatic amino acids such as phenylalanine, tyrosine and tryptophan; which leads onto vitamins and many secondary metabolites such as folates, ubiquinones and naphthoquines. It is believed to be rather specific in action and less toxic than other herbicides, because the shikimate pathway is not present in mammals and humans. However, glyphosate acts by preventing the binding of phosphoenol pyruvate to the active site of the enzyme, and phosphoenol pyruvate is a core metabolite present in all organisms; thus it has the potential to affect other metabolic pathways. This is borne out by many reports of toxicities associated with the herbicide reviewed in the Independent Science Panel Report, *The Case for a GM-free Sustainable World* [1].

An epidemiological study in the Ontario farming populations showed that glyphosate exposure nearly doubled the risk of late spontaneous abortions [2], and Prof. Eric-Giles Seralini and his research team from Caen University in France decided to find out more about the effects of the herbicide on cells from the human placenta.

They have now shown that glyphosate *is* toxic to human placental cells, killing a large proportion of them after 18 hr of exposure at concentrations below that in agricultural use [3]. Moreover, Roundup is always more toxic than its active ingredient, glyphosate; at least by two-fold. The effect increased with time, and was obtained with concentrations of Roundup 10 times lower than agricultural use.

The enzyme aromatase is responsible for making the female hormones estrogens from androgens (the male hormones). Glyphosate interacts with the active site of the enzyme but its effect on enzyme activity was minimal unless Roundup was present.

Interestingly, Roundup increased enzyme activity after 1 h of incubation, possibly because of its surfactant effect in making the androgen substrate more available to the enzyme. But at 18h incubation, Roundup invariably inhibited enzyme activity; the inhibition being associated with a decrease in mRNA synthesis,

suggesting that Roundup decreased the rate of gene transcription. Seralini and colleagues suggest that other ingredients in the Roundup formulation enhance the availability or accumulation of glyphosate in cells.

There is, indeed, direct evidence that glyphosate inhibits RNA transcription in animals at a concentration well below the level that is recommended for commercial spray application Transcription was inhibited and embryonic development delayed in sea urchins following exposure to low levels of the herbicide and/or the surfactant polyoxyethyleneamine. The pesticide should be considered a health concern by inhalation during spraying [4].

New research shows that a brief exposure to commercial glyphosate caused liver damage in rats, as indicated by the leakage of intracellular liver enzymes. In this study, glyphosate and its surfactant in Roundup were also found to act in synergy to increase damage to the liver [5].

Three recent case-control studies suggested an association between glyphosate use and the risk of non-Hodgkin lymphoma [6-8]; while a prospective cohort study in Iowa and North Carolina that includes more than 54 315 private and commercial licensed pesticide applicators suggested a link between glyphosate use and multiple myoeloma [9]. Myeloma has been associated with agents that cause either DNA damage or immune suppression. These studies did not distinguish between Roundup and glyphosate, and it would be important for that to be done.

There is now a wealth of evidence that glyphosate requires worldwide health warnings and new regulatory review. Meanwhile, its use should be reduced to a minimum as a matter of prudent precaution.

References

1. The Case for a GM-Free Sustainable World, Chapter 7, ISIS & TWN, London & Penang, 2003.
2. Savitz DA, Arbuckle , Kaczor D, Curtis KM. Male pesticide exposure and pregnancy outcome. *Am J Epidemiol* 2000, 146, 1025-36.
3. Richard S, Moslemi S, Sipahutar H, Benachour N and Seralini G-E. Differential effects of glyphosate and Roundup on human placental cells and aromatases
4. Marc J, Le Breton M, CormierP, Morales J, Belle´R and Mulner-Lorillo O. A glyphosate-based pesticide impinges on transcription. *Toxicology and Applied Pharmacology* 2005, 203, 1-8.
5. Benedetti AL, de Lourdes Vituri C, Trentin AG, Dominguesc MAC and Alvarez-Silva M. The effects of sub-chronic exposure of Wistar rats to the herbicide Glyphosate-Biocarb. *Toxicology Letters* 2004, 153, 227–32.
6. De Roos AH, Zahm SH, Cantor KP, et al. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. Occup Environ Med 2003, 60, E11 http://oem.bmjjournals.com/cgi/content/full/60/9/e11
7. Hardell L, Eriksson M, Nordstrom M. Exposure to pesticides as risk factor for non-Hodgkin's lymphoma and hairy cell leukemia: pooled analysis of two Swedish case-control studies. *Leuk Lymphoma* 2002, 43,1043–1049.
8. McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, Dosman JA, *et al*. 2001. Non-Hodgkin's lymphoma and specific pesticide exposures in men: cross-Canada study of pesticides and health. 2001, *Cancer Epidemiol Biomarkers Prev* 2001,10,1155–63.
9. De Roos AJ, Blair A, Rusiecki JA, Hoppin JA, Svec M, Dosemeci M, Sandler DP and Alavanja MC. Cancer incidence among glyphosate-exposed pesticide applicators in the agricultural health study. *Environ Health Perspect* 2005, 113, 49-54.