Glyphosate, the Active Ingredient in Roundup and its many formulations, and its “Inert Ingredients,” are Toxic to Humans and the Environment: A Brief Survey of Glyphosate Articles and Scientific Literature.

**Thesis:** Nearly all human chronic diseases are caused by the long-term, low-level, cumulative effects of exposure to environmental pollutants, many of which are toxins, toxicants or epitoxins.

**The Precautionary Principle:** When an activity raises threat of harm to human health or the environment, precautionary measures must be taken even if some cause and effect relationships are not fully established scientifically. The proponent of an activity, rather than the public, should bear the burden of proof. The process of applying the precautionary principle must be open, informed and democratic, and must include potentially affected parties. It must also involve an examination of the full range of alternatives, including no action.

**Relative toxicity of the components of the original formulation of Roundup to five North American anurans.**

Moore LJ, Fuentes L, Rodgers JH Jr, Bowerman WW, Yarrow GK, Chao WY, Bridges WC Jr.
Department of Forestry and Natural Resources, Clemson University, 261 Lehotsky Hall, Clemson, South Carolina 29634, USA.

The responses of five North American frog species that were exposed in an aqueous system to the original formulation of Roundup were compared. Carefully designed and un-confounded laboratory toxicity tests are crucial for accurate assessment of potential risks from the original formulation of Roundup to North American amphibians in aquatic environments. The formulated mixture of this herbicide as well as its components, isopropylamine (IPA) salt of glyphosate and the surfactant MON 0818 (containing polyethoxylated tallowamine (POEA)) were separately tested in 96 h acute toxicity tests with Gosner stage 25 larval anurans. Rana pipiens, R. clamitans, R. catesbeiana, Bufo Fowleri, and Hyla chrysoscelis were reared from egg masses and exposed to a series of 11 concentrations of the original formulation of Roundup herbicide, nine concentrations of MON 0818 and three concentrations of IPA salt of glyphosate in static (non-renewal) aqueous laboratory tests. LC50 values are expressed as glyphosate acid equivalents (ae) or as mg/L for MON 0818 concentrations for comparison between the formulation and components. R. pipiens was the most sensitive of five species with 96 h-LC50 values for formulation tests, for the five species, ranging from 1.80 to 4.22 mg ae/L, and MON 0818 exposures with 96 h-LC50 values ranging from 0.68 to 1.32 mg/L. No significant mortality was observed during exposures of 96 h for any of the five species exposed to glyphosate IPA salt at concentrations up to 100 times the predicted environmental concentration (PEC). These results agree with previous studies which have noted that the surfactant MON 0818 containing POEA contributes the majority of the toxicity to the herbicide formulations for fish, aquatic invertebrates, and amphibians. These study results suggest that anurans are among the most sensitive species, and emphasize the importance of testing the herbicide formulation in addition to its separate components to accurately characterize the toxicity and potential risk of the formulation.

**In vitro cytotoxic effect of glyphosate mixture containing surfactants**

Song HY, Kim YH, Seok SJ, Gil HW, Hong SY.
Department of Immunology, Soonchunhyang University College of Medicine, Cheonan, Korea.

We investigated whether glyphosate influences the cellular toxicity of the surfactants TN-20 and LN-10 on the mouse fibroblast-like cells, alveolar epithelial cells, and a heart cell line. The cytotoxicity of TN-20 and LN-10 (0.4-100 µM), in the presence or absence of glyphosate was determined by assessing membrane integrity. TN-20 toxicity was significantly lower in the presence of 50 μM glyphosate for the fibroblast-like cell (6.25 µM; 3.9% ± 3.4% vs -4.8% ± 0.7%), for the alveolar cells (0.78 µM; 5.7% ± 0.9% vs 0.1% ± 0.6%), and for the heart cell line.
(25.0 µM; 7.9% ± 3.0% vs 19.4% ± 0.7%) compared to that of TN-20 alone. The cellular toxicity of LN-10 towards the fibroblast-like cells was found to be increased in the presence of 50 µM glyphosate when LN-10 concentrations of 50 µM (31.3% ± 3.9% vs 19.2% ± 0.9%) and 100 µM (62.1% ± 3.4% vs 39.0% ± 0.7%) were compared to that of LN-10 alone. These results suggest that the mixture toxicity may be a factor in glyphosate-surfactant toxicity in patients with acute glyphosate herbicide intoxication.

Comparative toxicity of two glyphosate formulations (original formulation of Roundup and Roundup WeatherMAX) to six North American larval anurans

Fuentes L, Moore LJ, Rodgers JH Jr, Bowerman WW, Yarrow GK, Chao WY.
Department of Forestry and Natural Resources, Clemson University, Clemson, South Carolina, USA.
The toxicity of two glyphosate formulations (the original formulation of Roundup® and Roundup WeatherMAX®) to six species of North American larval anurans was evaluated by using 96-h static, nonrenewal aqueous exposures. The 96-h median lethal concentration values (LC50) ranged from 1.80 to 4.22 mg acid equivalent (ae)/L and 1.96 to 3.26 mg ae/L for the original formulation of Roundup and Roundup WeatherMAX, respectively. Judged by LC50 values, four species were more sensitive to Roundup WeatherMAX exposures, and two species were more sensitive to the original formulation. Two of six species, Bufo fowleri (p < 0.05, F = 14.89, degrees of freedom [df] = 1) and Rana clamitans (p < 0.05, F = 18.46, df = 1), had significantly different responses to the two formulations tested. Increased sensitivity to Roundup WeatherMAX likely was due to differences in the surfactants or relative amounts of the surfactants in the two formulations. Potency slopes for exposures of the original formulation ranged from 24.3 to 92.5% mortality/mg ae/L. Thresholds ranged from 1.31 to 3.68 mg ae/L, showing an approximately three times difference in the initiation of response among species tested. For exposures of Roundup WeatherMAX, slopes ranged from 49.3 to 84.2% mortality/mg ae/L. Thresholds ranged from 0.83 to 2.68 mg ae/L. Margins of safety derived from a simulated direct overspray were above 1, except for one species in exposures of Roundup WeatherMAX. Laboratory data based on aqueous exposures are conservative because of the lack of environmental ligands; however, these tests provide information regarding the relative toxicity between these two Roundup formulations.

The inside story on Monsanto and the glyphosate birth defect data

Claire Robinson 13th June 2011
The pesticide industry and regulators have repeatedly misled the public with claims that glyphosate is safe, says Claire Robinson. As a result, Monsanto's Roundup is used by gardeners and local authorities, in school grounds, and in farmers' fields. Industry and EU regulators knew as long ago as the 1980s-1990s that Roundup, the world's best selling herbicide, causes birth defects but they failed to inform the public. This is the conclusion of our new report, 'Roundup and birth defects: Is the public being kept in the dark?',* authored by a group of international scientists and researchers.
The report reveals that industry’s own studies (including one commissioned by Monsanto itself) showed as long ago as the 1980s that Roundup’s active ingredient glyphosate causes birth defects in laboratory animals. Industry submitted these studies to the European Commission in support of its application for glyphosate’s approval for use in Europe. As the ‘rapporteur’ member state for glyphosate, liaising between industry and the Commission, Germany took an active role in minimising the problems with glyphosate and must shoulder a chunk of the responsibility for allowing it onto the market.
The facts are these:

• Industry (including Monsanto) has known from its own studies since the 1980s that glyphosate causes malformations in experimental animals at high doses
• Industry has known since 1993 that these effects also occur at lower and mid doses
• The German government has known since at least 1998 that glyphosate causes malformations
• The EU Commission’s expert scientific review panel knew in 1999 that glyphosate causes malformations
• The EU Commission has known since 2002 that glyphosate causes malformations. This was the year it signed off on the current approval of glyphosate
But this information was not made public. On the contrary, the pesticide industry and Europe’s regulators have jointly misled the public with claims that glyphosate is safe. As a result, Roundup is liberally used by home gardeners and local authorities on roadsides, in school grounds, and other public areas, as well as in farmers’ fields. The latest whitewash attempt by regulators came in the wake of an independent scientific study published last year by Argentine scientists. The study showed that Roundup and glyphosate cause birth defects in frogs and chickens at concentrations much lower than those used in agricultural spraying. The research was prompted by reports of escalating levels of birth defects and cancers in areas of South America where glyphosate is heavily sprayed on genetically modified glyphosate-tolerant crops. After members of the European Parliament and NGOs raised concerns about the study, the German Federal Office for Consumer Protection and Food Safety, BVL, dismissed it with a claim that the ‘huge’ database of studies on glyphosate showed ‘no evidence of teratogenicity’ (ability to cause birth defects). Interestingly, BVL cited as proof of glyphosate’s safety the very same industry studies that our report reveals as showing evidence of teratogenicity. Our report shows how during the EU approval of glyphosate, the rapporteur Germany explained away the birth defects in the industry studies with bizarre excuses. For example, Germany creatively redefined a recognised skeletal malformation found in glyphosate-exposed animals as merely a ‘variation’. It repeatedly ‘disappeared’ findings of birth defects in glyphosate-exposed groups of animals by using historical control data – which have a wide variability because the experiments were performed under different conditions – instead of the valid control data from the experiment in hand. Welcome to the Alice-in-Wonderland world of pesticide regulation, where pesticide-induced birth defects are ‘variations’ and if you don’t like the findings of one experiment, you can borrow data from another to make them go away. The EU Commission’s expert review panel followed Germany in dismissing the birth defects, and the Commission signed off on the final approval of glyphosate in 2002. In response to our report, Monsanto published a statement on its website, claiming, 'Regulatory authorities and independent experts around the world agree that glyphosate does not cause adverse reproductive effects...or birth defects.' But this is the nub of the problem. Regulators are ‘agreeing’ that glyphosate is safe in clear contradiction of the scientific evidence before them. Monsanto also repeats the usual industry claim that the studies that show problems with glyphosate are ‘flawed’. But as our report proves, studies that show glyphosate causes birth defects include industry’s own, Monsanto’s among them. Is Monsanto saying its own studies are flawed? If so, we have all the more reason to worry, as these are the studies on which the current approval of glyphosate rests.

Commission delays review of glyphosate
A new pesticide regulation comes into force this June. It’s more stringent than the existing rules and an objective review of glyphosate under this new regulation may have resulted in a ban. This is partly because under the new regulation, independent (non-industry) studies have to be taken into consideration. Many independent studies, summarised in our report, show that glyphosate and Roundup cause birth defects, cancer, genetic damage, endocrine disruption, and other serious effects, often at low, realistic doses. Glyphosate was due to be reviewed in 2012. But late last year, after the Argentine study was presented to the EU Commission, the Commission quietly passed a directive delaying the review of glyphosate and 38 other pesticides until 2015. In 2015, glyphosate will be reviewed under lax, outdated standards. This is because the Commission has failed to complete the data requirements (the tests that industry has to do) for the new regulation in time for industry to do the new tests. Glyphosate will likely sail through its 2015 review and may not be reviewed under up-to-date, more stringent data requirements for another 15 years. So glyphosate could get a free regulatory ride until 2030, at a time when companies are applying to the EU for permission to cultivate genetically modified glyphosate-tolerant seeds in Europe. This would lead to a huge increase in the use of glyphosate, as has happened in North and South America. The beneficiary of the Commission’s delay will be the pesticide industry; the victim will be public health. We are asking the Commission to cancel the delay and conduct an immediate objective review of glyphosate and Roundup. In the meantime, it must use its powers to withdraw the herbicide from use in Europe.
Concerns about the best-selling herbicide Roundup are running at an all-time high. Scientific research published in 2010 showed that Roundup and the chemical on which it is based, glyphosate, cause birth defects in frog and chicken embryos at dilutions much lower than those used in agricultural and garden spraying. The EU Commission dismissed these findings, based on rebuttals provided by the German Federal Office for Consumer Protection and Food Safety, BVL. BVL cited unpublished industry studies to back its claim that glyphosate was safe. The Commission has previously ignored or dismissed many other findings from the independent scientific literature showing that Roundup and glyphosate cause endocrine disruption, damage to DNA, reproductive and developmental toxicity, neurotoxicity, and cancer, as well as birth defects. Many of these effects occur at very low doses, comparable to levels of pesticide residues found in food and the environment. This issue is of particular concern now that Monsanto and other producers of genetically modified seed are trying to get their glyphosate-tolerant crops approved for cultivation in Europe. In the EU Commission gives its approval, this will lead to a massive increase in the amount of glyphosate sprayed in the fields of EU member states, as has already happened in North and South America. Consequently, people’s exposure to glyphosate will increase. All these concerns could be addressed by an objective review of glyphosate and stringent new EU pesticide regulation due to come into force in June 2011. Just such a review was due to take place in 2012. However, shortly after the Commission was notified of the latest research showing that glyphosate and Roundup cause birth defects, it quietly passed a directive delaying the review of glyphosate and 38 other dangerous pesticides until 2015. This delay is being challenged in a lawsuit brought against the Commission by Pesticides Action Network Europe and Greenpeace. Delaying the review of glyphosate until 2015 is serious enough. But in reality, the Commission’s slowness in preparing the new data requirements for the incoming regulation mean that glyphosate may well not be re-assessed in the light of up-to-date science until 2030. The beneficiary will be the pesticide industry; the victim will be public health. The need for a review of glyphosate is particularly urgent in the light of the shortcomings of the existing review of the pesticide, on which its current approval rests. In this report, we examine the industry studies and regulatory documents that led to this approval. We show that industry and regulators knew as long ago as the 1980s and 1990s that glyphosate causes malformations – but that this information was not made public. We demonstrate how EU regulators reasoned their way from clear evidence of glyphosate’s teratogenicity in industry’s own studies (the same studies that BVL claimed show the safety of glyphosate) to a conclusion that minimized these findings in the EU Commission’s final review report. The German government and its agencies played a central role in this process. As the “rapporteur” member state for glyphosate, Germany was responsible for liaising between industry and the EU Commission and reporting the findings of industry studies. We show how Germany played down findings of serious harm in industry studies on glyphosate. It irresponsibly proposed a high “safe” exposure level for the public that ignored important data on glyphosate’s teratogenic effects. This level was accepted by the Commission and is now in force. Taken together, the industry studies and regulatory documents on which the current approval of glyphosate rests reveal that:

- Industry (including Monsanto) has known since the 1980s that glyphosate causes malformations in experimental animals at high doses
- Industry has known since 1993 that the side effects could also occur at lower and mid doses
- The German government has known since at least 1998 that glyphosate causes malformation
- The EU Commission’s expert scientific review panel knew in 1999 that glyphosate causes malformations
- The EU Commission has known since 2002 that glyphosate causes malformations.

This was the year its DG SANCO division published its final review report, laying out the basis for the current approval of glyphosate. The public, in contrast, has been kept in the dark by industry and regulators about the ability of glyphosate and Roundup to cause malformations. In addition, the work of independent scientists who have drawn attention to the herbicide’s teratogenic effects has been ignored, denigrated, or dismissed. These actions on the part of industry and regulators have endangered public health. They have also contributed to the growing division between independent and industry science, which in turn erodes public trust in the regulatory process. This report provides a comprehensive review of the peer-reviewed scientific literature, documenting the serious health hazards posed by glyphosate and Roundup herbicide formulations. On the basis of this
evidence, we call on the Commission to cancel its delay in reviewing glyphosate and to arrange an objective review of the pesticide. The review must take into account the full range of independent scientific literature, as demanded by the new pesticides regulation, and should be started as soon as the new data requirements are in place this year. In the meantime, the Commission should use its powers to withdraw glyphosate and Roundup from the market.

**Weed-Whacking Herbicide Proves Deadly to Human Cells**

Used in gardens, farms, and parks around the world, the weed killer Roundup contains an ingredient that can suffocate human cells in a laboratory, researchers say.

By Crystal Gammon and Environmental Health News | Tuesday, June 23, 2009

Used in yards, farms and parks throughout the world, Roundup has long been a top-selling weed killer. But now researchers have found that one of Roundup’s inert ingredients can kill human cells, particularly embryonic, placental and umbilical cord cells. The new findings intensify a debate about so-called “inerts” - the solvents, preservatives, surfactants and other substances that manufacturers add to pesticides. Nearly 4,000 inert ingredients are approved for use by the U.S. Environmental Protection Agency. Glyphosate, Roundup’s active ingredient, is the most widely used herbicide in the United States. About 100 million pounds are applied to U.S. farms and lawns every year, according to the EPA. Until now, most health studies have focused on the safety of glyphosate, rather than the mixture of ingredients found in Roundup. But in the new study, scientists found that Roundup’s inert ingredients amplified the toxic effect on human cells—even at concentrations much more diluted than those used on farms and lawns. One specific inert ingredient, polyethoxylated tallowamine, or POEA, was more deadly to human embryonic, placental and umbilical cord cells than the herbicide itself – a finding the researchers call “astonishing.” “This clearly confirms that the [inert ingredients] in Roundup formulations are not inert,” wrote the study authors from France’s University of Caen. “Moreover, the proprietary mixtures available on the market could cause cell damage and even death [at the] residual levels” found on Roundup-treated crops, such as soybeans, alfalfa and corn, or lawns and gardens. The research team suspects that Roundup might cause pregnancy problems by interfering with hormone production, possibly leading to abnormal fetal development, low birth weights or miscarriages. Monsanto, Roundup’s manufacturer, contends that the methods used in the study don’t reflect realistic conditions and that their product, which has been sold since the 1970s, is safe when used as directed. Hundreds of studies over the past 35 years have addressed the safety of glyphosate. “Roundup has one of the most extensive human health safety and environmental data packages of any pesticide that’s out there,” said Monsanto spokesman John Combest. “It’s used in public parks, it’s used to protect schools. There’s been a great deal of study on Roundup, and we’re very proud of its performance.” The EPA considers glyphosate to have low toxicity when used at the recommended doses. “Risk estimates for glyphosate were well below the level of concern,” said EPA spokesman Dale Kemery. The EPA classifies glyphosate as a Group E chemical, which means there is strong evidence that it does not cause cancer in humans. In addition, the EPA and the U.S. Department of Agriculture both recognize POEA as an inert ingredient. Derived from animal fat, POEA is allowed in products certified organic by the USDA. The EPA has concluded that it is not dangerous to public health or the environment. The French team, led by Gilles-Eric Seralini, a University of Caen molecular biologist, said its results highlight the need for health agencies to reconsider the safety of Roundup. “The authorizations for using these Roundup herbicides must now clearly be revised since their toxic effects depend on, and are multiplied by, other compounds used in the mixtures,” Seralini’s team wrote. Controversy about the safety of the weed killer recently erupted in Argentina, one of the world’s largest exporters of soy. Last month, an environmental group petitioned Argentina’s Supreme Court, seeking a temporary ban on glyphosate use after an Argentine scientist and local activists reported a high incidence of birth defects and cancers in people living near crop-spraying areas. Scientists there also linked genetic malformations in amphibians to glyphosate. In addition, last year in Sweden, a scientific team found that exposure is a risk factor for people developing non-Hodgkin lymphoma. Inert ingredients are often less scrutinized than active pest-killing ingredients. Since specific herbicide formulations are protected as trade secrets, manufacturers aren’t required to publicly disclose them. Although Monsanto is the largest manufacturer of glyphosate-based herbicides, several other manufacturers sell similar herbicides with different inert ingredients.
ingredients. The term “inert ingredient” is often misleading, according to Caroline Cox, research director of the Center for Environmental Health, an Oakland-based environmental organization. Federal law classifies all pesticide ingredients that don’t harm pests as “inert,” she said. Inert compounds, therefore, aren’t necessarily biologically or toxicologically harmless — they simply don’t kill insects or weeds. Kemery said the EPA takes into account the inert ingredients and how the product is used, whenever a pesticide is approved for use. The aim, he said, is to ensure that “if the product is used according to labeled directions, both people’s health and the environment will not be harmed.” One label requirement for Roundup is that it should not be used in or near freshwater to protect amphibians and other wildlife. But some inert ingredients have been found to potentially affect human health. Many amplify the effects of active ingredients by helping them penetrate clothing, protective equipment and cell membranes, or by increasing their toxicity. For example, a Croatian team recently found that an herbicide formulation containing atrazine caused DNA damage, which can lead to cancer, while atrazine alone did not. POEA was recognized as a common inert ingredient in herbicides in the 1980s, when researchers linked it to a group of poisonings in Japan. Doctors there examined patients who drank Roundup, either intentionally or accidentally, and determined that their sicknesses and deaths were due to POEA, not glyphosate. POEA is a surfactant, or detergent, derived from animal fat. It is added to Roundup and other herbicides to help them penetrate plants’ surfaces, making the weed killer more effective. “POEA helps glyphosate interact with the surfaces of plant cells,” explained Negin Martin, a scientist at the National Institute of Environmental Health Sciences in North Carolina, who was not involved in the study. POEA lowers water’s surface tension—the property that makes water form droplets on most surfaces—which helps glyphosate disperse and penetrate the waxy surface of a plant. In the French study, researchers tested four different Roundup formulations, all containing POEA and glyphosate at concentrations below the recommended lawn and agricultural dose. They also tested POEA and glyphosate separately to determine which caused more damage to embryonic, placental and umbilical cord cells. Glyphosate, POEA and all four Roundup formulations damaged all three cell types. Umbilical cord cells were especially sensitive to POEA. Glyphosate became more harmful when combined with POEA, and POEA alone was more deadly to cells than glyphosate. The research appears in the January issue of the journal Chemical Research in Toxicology. By using embryonic and placental cell lines, which multiply and respond to chemicals rapidly, and fresh umbilical cord cells, Seralini’s team was able to determine how the chemicals combine to damage cells. The two ingredients work together to “limit breathing of the cells, stress them and drive them towards a suicide,” Seralini said. The research was funded in part by France’s Committee for Research and Independent Information on Genetic Engineering, a scientific committee that investigates risks associated with genetically modified organisms. One of Roundup’s primary uses is on crops that are genetically engineered to be resistant to glyphosate. Monsanto scientists argue that cells in Seralini’s study were exposed to unnaturally high levels of the chemicals. “It’s very unlike anything you’d see in real-world exposure. People's cells are not bathed in these things,” said Donna Farmer, another toxicologist at Monsanto. Seralini’s team, however, did study multiple concentrations of Roundup. These ranged from the typical agricultural or lawn dose down to concentrations 100,000 times more dilute than the products sold on shelves. The researchers saw cell damage at all concentrations. Monsanto scientists also question the French team’s use of laboratory cell lines. “These are just not very good models of a whole organism, like a human being,” said Dan Goldstein, a toxicologist with Monsanto. Goldstein said humans have protective mechanisms that resist substances in the environment, such as skin and the lining of the gastrointestinal tract, which constantly renew themselves. “Those phenomena just don’t happen with isolated cells in a Petri dish.” But Cox, who studies pesticides and their inert ingredients at the Oakland environmental group, says lab experiments like these are important in determining whether a chemical is safe. “We would never consider it ethical to test these products on people, so we’re obliged to look at their effects on other species and in other systems,” she said. “There's really no way around that.” Seralini said the cells used in the study are widely accepted in toxicology as good models for studying the toxicity of chemicals. “The fact is that 90 percent of labs studying mechanisms of toxicity or physiology use cell lines,” he said. Most research has examined glyphosate alone, rather than combined with Roundup’s inert ingredients. Researchers who have studied Roundup formulations have drawn conclusions similar to the Seralini group’s. For example, in 2005, University of Pittsburg ecologists added Roundup at the manufacturer’s recommended dose to ponds filled with frog and toad tadpoles. When they returned two weeks...
later, they found that 50 to 100 percent of the populations of several species of tadpoles had been killed. A group of over 250 environmental, health and labor organizations has petitioned the EPA to change requirements for identifying pesticides’ inert ingredients. The agency’s decision is due this fall. “It would be a big step for the agency to take,” said Cox. “But it’s one they definitely should.” The groups claim that the laws allowing manufacturers to keep inert ingredients secret from competitors are essentially unnecessary. Companies can determine a competitor’s inert ingredients through routine lab analyses, said Cox. “The proprietary protection laws really only keep information from the public,” she said. This article originally ran at Environmental Health News, a news source published by Environmental Health Sciences, a nonprofit media company.

**Safety Review of Glyphosate Herbicide Faces Tough Critics**

*By Deniza Gertsberg | Nov 21, 2011*

Glyphosate, the non-selective herbicide that is the active ingredient in Monsanto’s Roundup formula, is up for a routine safety review in the United States and Canada. The herbicide has been used in eliminating weeds in soybeans, corn, cotton, as well as for lawn and garden maintenance since the early 1970s. “More than 2 billion lbs of herbicide were used globally in 2007, with one quarter of that total – 531 million lbs – used in the United States in that timeframe, according to a report issued in February by the EPA,” recently reported Reuters. Since at least 1996, the thirst for glyphosate was fueled in large measure by the development of glyphosate tolerant crops (e.g., Monsanto’s Roundup Ready lines), which are able to withstand continued application of this herbicide. As more genetically engineered crops are planted, more glyphosate is used. For example, 94% of soybeans, planted on 75.2 million acres in 2011, were genetically engineered. With the government’s encouragement, in the form of subsidies for crops like soybean, corn and cotton, the nation’s glyphosate addiction intensified. In the meantime, concerns about the impact of glyphosate on human and animal health and the environment are growing. Many scientists are alarmed, for example, about the links between glyphosate and birth defects, cancer, impact on wildlife, and environmental damage. The Center For Food Safety (“Center”) recently noted in its August 3, 2011, letter to the U.S. Secretary of Agriculture, Tom Vilsack, that: Roundup Ready crop systems has decimated populations of milkweed in the agricultural fields of Iowa and likely other Midwestern states. This has contributed (along with other factors) to the 15-year decline in Monarch butterflies that require milkweed as a host plant for larvae (caterpillars). Additionally, due to weed resistance caused by over reliance on glyphosate, farmers need more glyphosate and often more toxic chemicals like 2,4-D, dicamba and atrazine to control weeds (a.k.a. “superweeds”).

The Center noted that:

- Glyphosate-resistant crop systems have triggered an epidemic of glyphosate-resistant weeds, which constitute one of the most serious challenges facing American farmers. Agronomists have recently sounded the alarm about weeds resistant to multiple herbicides (usually including glyphosate).

- Glyphosate-resistant crop systems have triggered an epidemic of glyphosate-resistant weeds, which constitute one of the most serious challenges facing American farmers. Agronomists have recently sounded the alarm about weeds resistant to multiple herbicides (usually including glyphosate).

The Institute of Science in Society has called for a global ban on glyphosate. Professor Don Huber, expressing his concern about the impact of glyphosate on soil, wrote in his public comments to the EPA, that “[b]oth the short- and long-term effects of glyphosate on soil biology are becoming serious concerns for crop production efficiency and food safety,” because the herbicide can “affect the physiological availability of nutrients for plants, and reduces nutrient availability and uptake from soil.” Similarly, Jeffrey Smith, a long-time consumer advocate, noted that: The glyphosate molecule deprives crops of the vital minerals necessary for healthy functioning, and especially the ability to resist soilborne diseases. It annihilates soil organisms that live around the roots and help suppress disease. And it is highly toxic to plants. But the clincher is that it dramatically promotes disease-causing organisms, present in almost all soils, which overrun the weakened crops with deadly infections. During the EPA’s review the agency said that it plans to re-evaluate the “risks from glyphosate and certain inert ingredients to humans and the environment...” Similarly, Health Canada Pest Management Regulatory Agency pesticide re-evaluation program will consider the potential risks as well as the value of
pesticide products to “ensure they meet modern standards established to protect human health and the environment.” The EPA is collecting data until summer of 2012 and a decision is expected by 2015. The Health Canada Pest Management Regulatory Agency reported that its target date for completion of glyphosate review is 2014.

**Comparative effects of the formulation of glyphosate-surfactant herbicides on hemodynamics in swine**


Lee HL, Kan CD, Tsai CL, Liou MJ, Guo HR.
Graduate Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

Most of the glyphosate-surfactant herbicides (GlySH) are formulated commercial products containing isopropylamine (IPA) salt of glyphosate (IPAG), variable amount of a surfactant, and water. Although glyphosate is only slightly toxic to rats, ingestion of GlySH may lead to severe effects, including death, in humans. We conducted a study to evaluate the cardiovascular effects of the components of GlySH. We used five groups of male piglets, each receiving infusion of normal saline (control), glyphosate in NaOH base, IPA, IPAG, and polyoxyethyleneamine (POEA), respectively. We chose concentrations that are similar to those in the commonly used GlySH (41% of IPAG and 15% surfactant). We found that IPAG reduced the mean arterial blood pressure (MABP) and left-ventricular stroke work index (LVSWI) during the infusion, but both recovered gradually. It also decreased the cardiac index but increased the pulmonary capillary wedge pressure, central venous pressure (CVP), and mean pulmonary arterial pressure (MPAP). POEA infusion reduced the cardiac index and LVSWI, but not the MABP. It also increased the pulmonary capillary wedge pressure, CVP, MPAP, and pulmonary vascular resistance index. IPA increased the MABP, which was higher than those in the control, IPAG, and POEA groups. Glyphosate in NaOH base infusion did not affect the hemodynamics but slightly reduced the blood pH and base excess (BE) values. POEA and IPAG also resulted in metabolic acidosis, with lactate formation and decreased BE values. We conclude that both POEA and IPAG infusion affected hemodynamics and resulted in death in piglets, whereas glyphosate (NaOH base) had no similar effects.

**Glyphosate poisoning**

*Toxicol Rev. 2004;23(3):159-67.*

Bradberry SM, Proudfoot AT, Vale JA.
National Poisons Information Service (Birmingham Centre) and West Midlands Poisons Unit, City Hospital, Birmingham, UK.

Glyphosate is used extensively as a non-selective herbicide by both professional applicators and consumers and its use is likely to increase further as it is one of the first herbicides against which crops have been genetically modified to increase their tolerance. Commercial glyphosate-based formulations most commonly range from concentrates containing 41% or more glyphosate to 1% glyphosate formulations marketed for domestic use. They generally consist of an aqueous mixture of the isopropylamine (IPA) salt of glyphosate, a surfactant, and various minor components including anti-foaming and colour agents, biocides and inorganic ions to produce pH adjustment. The mechanisms of toxicity of glyphosate formulations are complicated. Not only is glyphosate used as five different salts but commercial formulations of it contain surfactants, which vary in nature and concentration. As a result, human poisoning with this herbicide is not with the active ingredient alone but with complex and variable mixtures. Therefore, It is difficult to separate the toxicity of glyphosate from that of the formulation as a whole or to determine the contribution of surfactants to overall toxicity. Experimental studies suggest that the toxicity of the surfactant, polyoxyethyleneamine (POEA), is greater than the toxicity of glyphosate alone and commercial formulations alone. There is insufficient evidence to conclude that glyphosate preparations containing POEA are more toxic than those containing alternative surfactants. Although surfactants probably contribute to the acute toxicity of glyphosate formulations, the weight of evidence is against surfactants potentiating the toxicity of glyphosate. Accidental ingestion of glyphosate formulations is generally associated with only mild, transient, gastrointestinal features. Most reported cases have followed the deliberate ingestion of the concentrated formulation of Roundup (The use of trade names is for product identification purposes only and does not imply endorsement.) (41% glyphosate as the IPA salt and 15% POEA). There is a
reasonable correlation between the amount ingested and the likelihood of serious systemic sequelae or death. Advancing age is also associated with a less favourable prognosis. Ingestion of >85 mL of the concentrated formulation is likely to cause significant toxicity in adults. Gastrointestinal corrosive effects, with mouth, throat and epigastric pain and dysphagia are common. Renal and hepatic impairment are also frequent and usually reflect reduced organ perfusion. Respiratory distress, impaired consciousness, pulmonary oedema, infiltration on chest x-ray, shock, arrhythmias, renal failure requiring haemodialysis, metabolic acidosis and hyperkalaemia may supervene in severe cases. Bradycardia and ventricular arrhythmias are often present pre-terminally. Dermal exposure to ready-to-use glyphosate formulations can cause irritation and photo-contact dermatitis has been reported occasionally; these effects are probably due to the preservative Proxel (benzisothiazolin-3-one). Severe skin burns are very rare. Inhalation is a minor route of exposure but spray mist may cause oral or nasal discomfort, an unpleasant taste in the mouth, tingling and throat irritation. Eye exposure may lead to mild conjunctivitis, and superficial corneal injury is possible if irrigation is delayed or inadequate. Management is symptomatic and supportive, and skin decontamination with soap and water after removal of contaminated clothing should be undertaken in cases of dermal exposure.

**Glyphosate--a non-toxic pesticide?**
Pieniazek D, Bukowska B, Duda W.
Katedry Biofizyki Skazań Srodowiska Uniwersytetu Łódzkiego.
Glyphosate is currently the most commonly applied herbicide and its use is still growing. Nowadays, over 50 commercial preparations containing this compound are used, and these formulations are much more toxic than their active compound, glyphosate, owing to the presence of many surfactants and carrier compounds. Toxicological investigations provide evidence that glyphosate is an extremely "safe" herbicide for animals. This is why its use in agriculture is universal. In June 1991, the Environmental Protection Agency (EPA) categorized this compound into class E (according to EPA there are five categories of carcinogenicity), which means that it is probably not carcinogenic to humans. Unfortunately, the study carried out by Swedish oncologists in 2001 showed that glyphosate may induce cancer of the lymphatic system. The results of the Swedish study have changed our opinion about "safety" of this herbicide. Investigations concerning both its accumulation and toxic effect in animals and plants are now under way in many laboratories.

**Safety evaluation and risk assessment of Roundup and its active ingredient, glyphosate, for humans**
Williams GM, Kroes R, Munro IC.
Department of Pathology, New York Medical College, Valhalla 10595, USA.
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.

Richard C. Honour, PhD
Executive Director
March 11, 2013