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OVERVIEW OF RESEARCH FINDINGS

"Long-term Toxicity of a Roundup Herbicide and a Roundup-Tolerant Genetically Modified Maize"
Gilles-Eric Seralini, Emilie Clair, Robin Mesnage, Steeve Gress, Nicolas Defarge, Manuela Malatesta, Didier Hennequin, and Joel Spiroux de Vendomois,
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THE RESEARCH STUDY

This is the first long-term peer reviewed toxicity study into the health impact of a GM tolerant maize crop and the world's most popular herbicide, Roundup. The research shows that consuming even relatively low levels of the commercial NK603 Roundup tolerant GM maize or of the herbicide, Roundup, can result in greatly increased levels of mammary tumors, kidney and liver damage, and premature death in laboratory rats.

The study was conducted over two years - the lifespan of a rat. The scientists explain that currently all edible agricultural GM crop foods are approved safe on the basis of 90-day feeding trials. (This is equivalent to late teenage years/early adulthood in a rat.) They also state that only the active principle in Roundup, glyphosate, has been tested and not the commercial formulation.

The trial was designed to study any adverse long-term effects resulting from feeding rats on relatively low levels of the commercial GM maize NK603 and Roundup, both individually and combined. Doses of Roundup started within the range of levels permitted by regulatory authorities in drinking water and as chemical residues in GM feed. Doses of NK603 were consistent with those used in previous Monsanto studies.

Researchers found that even consuming low levels of NK603 and Roundup, separately or combined, can cause serious health problems, but these only became apparent when the rats were older than 90 days. The first tumor was observed after 120 days, but the majority were only detected after 18 months.

The research was conducted by a team of scientists led by molecular biologist and endocrinologist, Professor Gilles-Eric Seralini, co-director of the Risk Quality and Sustainable Environment Unit at the University of Caen, France, who is an authority on studies into the health impact of GMOs and pesticides. It was supported by the independent research organization, CRIIGEN.

Trial Methodology

- The trial studied the long-term effects of NK603 GM corn and Roundup, individually and combined, on the health of rats over two years, their entire lifetime.
- The study was carried out using two hundred rats fed a standard balanced diet. They were divided into ten groups each containing ten males and ten females.

- Three groups tested the effect of NK603 alone. Each group had a different proportion of NK603 in their feed starting at 11%, then 22% and finally 33% of their total diet.
- Three groups tested the effect of NK603, which had been sprayed with Roundup in the field at the same proportions of 11%, 22 % and 33% of their total diet.

- Three groups tested the effect of Roundup alone, administered via their drinking water at three different concentrations with one control group.
  - The lowest level corresponded to contamination found in some tap water.
  - The intermediate level corresponded to the maximum level permitted in the US in GM feed
  - The highest level was half the strength of Roundup when diluted for use in agriculture.
  - The control group was fed a diet containing 33% of non-GM corn and plain drinking water.
- The researchers took blood and urine samples for analysis monthly for the first three months and then every three months and at the end of the trial studied the rats' principal organs.

Results of the Trial

- The study shows that both NK603 GM maize and Roundup can cause severe adverse health effects including mammary tumors and kidney and liver damage, leading to premature death.
- It found that the NK603 GM maize and Roundup both caused similar damage to the rats' health, whether they were used separately or together.
- Researchers identified a "threshold effect" where even the lowest doses were associated with severe health problems.
- Up to 50% of males and 70% of females died prematurely, before deaths could be put down to normal ageing, compared with only 30% and 20% in the control group.
- Females developed fatal mammary tumors and pituitary disorders. Males suffered liver damage, developed kidney and skin tumors and problems with their digestive system.
- The severe health outcomes only started to appear after the first 90 days. The first large detectable tumors – larger than 17.5mm in females and 20mm in males - appeared after four and seven months in males and females respectively, but only after 14 months in the female control group and 23 months in a control male. However, the majority of tumors were only detected from 18 months onwards.
- By the 24th month, 50% - 80% of the females had developed large tumors compared to 30% in the control group.
- The largest tumors were five times more frequent in females than in males and 93% were mammary tumors.
- The tumors "were deleterious to health due to a very large size", making it difficult for the rats to breathe, causing problems with their digestion and resulting in haemorrhaging.
- By the end of the trial, on average, researchers found twice as many large tumors among males in the treated groups as in the control group. Only one tumor appeared in the control group, in the 23rd month. Treated males suffered severe liver and kidney dysfunction. Liver congestions and necrosis were 2.5 to 5.5 times higher than in the control group. There were also 1.3 – 2.3 times more instances of "marked and severe" kidney disease.
- In all treated groups, there were 2 – 3 times more deaths amongst the females compared to the controls by the end of the experiment.
- Across all treatments and both sexes, researchers found 2 - 3 times more large tumors than in the control group.

The paper states: “Similar degrees of pathological symptoms were noticed in this study to occur from the lowest to the highest doses suggesting a threshold effect. This corresponds to levels likely to arise from consumption or environmental exposure, such as either 11% GM maize in food, or 50ng/L of glyphosate in R-formulation [the lowest concentration of Roundup in the rats’ drinking water] as can be found in some contaminated drinking tap waters, and which falls within authorized limits.”

Assessment of Trial Findings

- The lowest dose tested in the study (50 nanograms per liter) is below safety limits for glyphosate in water and crops. EU legislation sets the maximum permitted concentration (MPC) in water at 0.1 ⌈g/liter, 1 mg/kg in maize, and 20 mg/kg in other animal feeds like soy, oats and barley. The US sets a Maximum Residual Level (MRL) in some animal feed of 400mg/kg.
- The researchers hypothesize that the reason why NK603, NK603 sprayed with Roundup, and Roundup on its own, all produced very similar negative health outcomes, is that both the GM maize and the weedkiller Roundup “may cause hormonal disturbances in the same biochemical and physiological pathway.”
- Although previous research has shown that glyphosate, the active ingredient in the herbicide Roundup and a known endocrine disruptor, can cause liver and kidney failure if consumed above maximum permitted residue levels, this is the first research that suggests that even very low levels, such as those found in some drinking water and in the food chain, are harmful.
- The paper says: “The results of the study presented here clearly demonstrate that lower levels of complete agricultural glyphosate herbicide formulations, at concentrations well below officially set safety limits, induce severe hormone-dependent mammary, hepatic [liver] and kidney disturbances.” It suggests that overexpression of the GM “transgene” EPSPS, which makes NK603 tolerant to Roundup in the field, may disrupt biosynthetic pathways and cause similar problems. Most edible GM crops use EPSPS to make them tolerant to Roundup.
- The researchers also suggest that there should be long-term feeding studies of the commercial formulation of pesticides and not simply on their active ingredient. Roundup was approved for use on the basis of tests of only its active ingredient, glyphosate. However, the commercial formulation includes ingredients which enable the glyphosate to penetrate plants more efficiently. Consequently the tests did not reveal the long-term effects of low dose exposure of the commercial product on farms, feed, food and water.
- The researchers note that animal feeding trials are not required by regulators before granting approval for commercial use in GM crops. However, several 90-day rat-feeding trials have been carried out by the biotechnology companies seeking approval of their products under guidelines set out by the Organization for Economic Cooperation and Development.
- The researchers believe that long-term studies are needed to evaluate the safety of GM crops. Currently all GM food crops have been approved safe on the basis of 90-day feeding studies in mammals.

Regulatory Implications and Need for Further Research

The research outcomes call into question the adequacy of the current regulatory process, which has been used to license all new industrial chemicals, pesticides and other ‘novel crops’ since the Second World War.

It also highlights the urgent need for more long-term studies to evaluate the safety of all GM food crops, which are currently grown on almost ten percent of the world’s arable land. Currently all GM food crops

have been approved safe on the basis of 90-day feeding studies in mammals. However, the first large tumour was only observed four months into the trial and most were not detected until after 18 months.

Copies of the research can be obtained on request from CRIIGEN: www.criigen.org and from Food and Chemical Toxicology www.journals.elsevier.com/food-and-chemical-toxicology/

APPENDIX: Background Information

Professor Seralini approached The Sustainable Food Trust to help communicate the results of the study on a global scale with Dr Michael Antoniou who is a Member of the CRIIGEN Scientific Council.

CRIIGEN - Committee of Research and Independent Information on Genetic Engineering
The Committee of Research and Independent Information on Genetic Engineering (CRIIGEN) is a non-profit organization set up by Professor Gilles-Eric Seralini, Professor of Molecular Biology at Caen University, and former ecology minister Corinne Lepage MEP, to offer scientific expertise on pollutants to health and environment. It is particularly focused on GMO's and their impact on agriculture, food, medicine and human health. Professor Seralini was in charge of risk assessment for two government commissions and has advised the European Commission, Parliament and Councils and a number of governments on the commercial use of GMO's.

Since its establishment, CRIIGEN have campaigned for more transparency in the genetic engineering trials carried out by commercial organisations, the biotech companies. It also lobbies the governments to improve the quality of risk assessment for GMO's.

Previous research by CRIIGEN has included reanalysing existing studies into GM crops. One of these in 2007 concluded that the GM crop, MON 863, adversely affected liver and kidney function in rats. A further reanalysis of three more industry studies in 2009, reaffirmed CRIIGEN's results regarding the crop's toxicity. In 2011 CRIIGEN published a review of 19 published reports on animal GM feeding studies, which found that kidney and liver problems can arise even in 90-day trials. This has become a seminal work and the most consulted report on the topic, downloaded by more than 60,000 scientists from the SpringerOpen databank.

Professor Gilles Eric Séralini – Professor of Molecular Biology and President of the Scientific Board at Committee of Independent Research and Information on Genetic Engineering (CRII-GEN)
Gilles Eric Seralini is Professor of Molecular Biology and co-director of the Risk Quality and Sustainable Environment Unit at Caen University, France, and an expert on pesticides, pollutants and the effects of GMO's on health. As a result of his research work into cancer and the disruptors of reproduction, he started to investigate possible pollutants in air, water and food.

He established CRIIGEN – Committee of Independent Research and Information on Genetic Engineering – in order to conduct more thorough scientific research into GMO's. He is now the President of the Scientific Board.

Professor Seralini was in charge of risk assessment for two French governmental commissions to evaluate GM food and in 2003 he was appointed as an expert for the European Commission to prepare the defence case for the moratorium on commercial GMO's against the US/Canada and Argentina.

He has written more than 100 scientific articles and conference papers for international symposiums and spoken globally about the impact of GM food and pesticides on animal and human health. In 2011, he

was involved in a high profile law trial where he sued researchers from the French Association of Plant Biotechnologies (AFBV) for defamation when they tried to discredit his reanalysis of Monsanto trials. The court in Paris ruled in his favour.

Dr Michael Antoniou – Reader in Molecular Genetics, Kings College, London School of Medicine, and Member, CRIIGEN Scientific Council

Dr Michael Antoniou is an expert in genetic science including GM technologies. He has worked as a molecular biologist for 32 years using genetic engineering technology to investigate gene organization and control. He holds a degree in Biochemistry from the University of Oxford, a PhD in Molecular Biology from Reading and has over 50 peer-reviewed publications of original work.

For the last 18 years he has run an independent medical research team at Guys' Hospital in London. Their work has helped to contribute to gene therapy medicines for diseases such as muscular dystrophy, thalassemia and immune dysfunction.

Dr Antoniou first became concerned about the widespread commercial use of genetically modified organisms (GMOs) in 1995 when industry experts started claiming it was a precise technology with a predictable outcome. He has spoken at international conferences and in the press about his concerns about GMOs for the last fifteen years. He believes the feeding trials currently used to evaluate and license GM crops in Europe are inadequate and in urgent need of review.

Dr Antoniou warns that GMO's are not only highly unpredictable but could give rise to the unexpected production of toxins and allergens in food, problems that are unlikely to be highlighted by the current research procedures which precede regulatory approval.

The Sustainable Food Trust

The Sustainable Food Trust was set up by former director of the Soil Association, Patrick Holden. The charity aims to bring together the many groups and individuals working internationally in this area to help transform our present food system and meet the multiple challenges of climate change, resource depletion, food security and population growth. One of its particular areas of interest is comparing different systems of agriculture and their impact on human and environmental health.