Effects of neonicotinoid insecticides on mammalian nicotinic acetylcholine receptors.

Tomizawa, M, Lee, D.L., Casida, J.E. Neonicotinoid insecticides: Molecular Features Conferring Selectivity for Insect versus Mammalian Nicotinic Receptors. *J. Agric. Food Chem*. **48** (12), 6016-6024 (2000). *These authors showed that neonicotinoids acted on mammalian nicotinic acetylcholine receptors as well, but considered that the selective nature of its binding (i.e. less affinity than in insects) made it safe for human exposure.*

Tennekes, H.A. The significance of the Druckrey-Küpfmuller equation for risk assessment – The toxicity of neonicotinoid insecticides to arthropods is reinforced by exposure time. *Toxicology* **276**, 1-4 (2010). *Tennekes was the first to prove that neonicotinoids can produce effects at any concentration level, provided the exposure time is sufficiently long.*

Tennekes, H.A., Sánchez-Bayo, F. Time-Dependent Toxicity of Neonicotinoids and Other Toxicants: Implications for a New Approach to Risk Assessment. *J. Environment. Analytic. Toxicol.* S4:001. doi:10.4172/2161-0525.S4-001 (2011). *Tennekes and Sánchez-Bayo demonstrated that chemicals that bind irreversibly to specific receptors (neonicotinoids, genotoxic carcinogens and some metals) will produce toxic effects in a time-dependent manner, no matter how low the level of exposure.*

Duzguner, V., Edogaan, S. Acute oxidant and inflammatory effects of *imidacloprid* on the mammalian central nervous system and liver in rats. *Pest. Biochem. Physiol.* **97**, 13-18 (2010). *Imidacloprid has acute oxidant and inflammatory effects on the mammalian CNS and liver.*

Kimura-Kuroda J., Hayashi, M., Kawano, H. Nicotine-like effects of neonicotinoids on rat cerebellar neurons. *Neuroscience Research*, **71**, suppl, (2011). *This is a study to determine to what extent the neonicotinoids imidacloprid and acetamiprid affected the nAChRs of rat cerebellar neurons and to compare their effects with nicotine by using in vitro excitatory Ca-influx assay. Although nicotine excited rather higher proportions of neurons and produced a higher peak of Ca-influx compared with the two neonicotinoids, both had higher binding to the neurons and were significantly inhibited with nAChR antagonists. The authors suggested that the neonicotinoids could have adverse effects on human health, especially in the developing foetus.*

Bal, R. *et al.* Insecticide imidacloprid induces morphological and DNA damage through oxidative toxicity on the reproductive organs of developing male rats. *Cell. Biochem. Funct.* (2012) DOI: 10.1002/cbf.2826. *The weights of the epididymis, vesicula seminalis, epididymal sperm concentration, body weight gain, testosterone and reduced glutathione values were lower in the imidacloprid-treated groups than that in the controls. All treated groups had increased lipid peroxidation, fatty acid concentrations and higher rates of abnormal sperm. Apoptosis and fragmentation of seminal DNA were higher in rats treated at the two higher doses of imidacloprid. These results show that imidacloprid has a negative effect on sperm and testis of rats.*

Bal, R. *et al*. Effects of clothianidin exposure on sperm quality, testicular apoptosis and fatty acid composition in developing male rats. *Cell. Biol. Toxicol.* DOI 10.1007/s10565-012-9215-0. *It is concluded that low doses of clothianidin exposure during critical stages of sexual maturation had moderate detrimental effects on reproductive organ system and more*

severe effects are likely to be observed at higher dose levels. In addition, the reproductive system may be more sensitive to exposure of clothianidin even earlier in development (prenatal and early postnatal), and therefore it could be expected that more severe effects could also be observed at the NOAEL dose levels, if dosing had occurred in utero or early postnatal.

Abou-Donia, M.B. *et al*. Imidacloprid induces neurobehavioral deficits and increases expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats following in utero exposure. *J. Toxicol. Environ. Health A*. 2008; 71 (2) 119-130. *Gestational exposure to a single large, non-lethal, dose of imidacloprid produces significant neurobehavioral deficits an and increased expression of glial fibrillary acidic protein in several brain regions of the offspring on postnatal day 30, corresponding to human early adolescent age. These changes may have long-term adverse effects in the offspring.*

Li, P., Ann, J., Akk, G. Activation and Modulation of Human α4β2 Nicotinic Acetylcholine Receptors by the Neonicotinoids Clothianidin and Imidacloprid. *J. Neuroscience Research* DOI:10.1002/jnr.22644 (2011). *Since the clinical manifestations of neonicotinoid poisoning clearly involved the nicotinic receptors, studies of the effects of clothianidin and imidacloprid on human neuronal-type α4β2 nAChRs were undertaken. Both chemicals had effects on human receptors, but imidacloprid more so than clothianidin*.

Mondal, S., Ghosh, R.C., Mate, M.S., Karmakar, D.P. Effects of Acetamiprid on Immune System in Female Wistar Rats. *Proc. Zool. Soc*. **62** (2), 109-117 (2009).
A subacute toxicity study of acetamiprid was undertaken in 72 female wistar rats in four groups (18 each). Three different concentrations of acetamiprid (25, 100 and 200 mg/kg of body weight) were administered orally to rats. The results indicated that acetamiprid suppressed both CMI and antibody forming ability of lymphocytes.

Calderon-Segura, M.E. *et al*. Evaluation of Genotoxic and Cytotoxic Effects in Human Peripheral Blood Lymphocytes Exposed *in Vitro* to Neonicotinoid Insecticides *Journal of Toxicology* Volume 2012, Article ID 612647, doi:10.1155/2012/612647
Abstract: *Calypso (thiacloprid), Poncho (clothianidin), Gaucho (imidacloprid), and Jade (imidacloprid) are commercial neonicotinoid insecticides, a new class of agrochemicals in Mexico. However, genotoxic and cytotoxic studies have not been performed. In the present study, human peripheral blood lymphocytes (PBL) were exposed in vitro to different concentrations of the four insecticides. The genotoxic and cytotoxic effects were evaluated using the alkaline comet and trypan blue dye exclusion assays. DNA damage was evaluated using two genotoxicity parameters: tail length and comet frequency. Exposure to 9.5 $\times 10^{-6}$ to 5.7 $\times 10^{-5}$ M Jade; 2.8 $\times 10^{-4}$ to 1.7 $\times 10^{-3}$ M Gaucho; 0.6 $\times 10^{-1}$ to 1.4 $\times 10^{-1}$ M Calypso; 1.2 $\times 10^{-1}$ to 9.5 $\times 10^{-1}$ M Poncho for 2 h induced a significant increase DNA damage with a concentration-dependent relationship. Jade was the most genotoxic of the four insecticides studied. Cytotoxicity was observed in cells exposed to 18 $\times 10^{-3}$ M Jade, 2.0 $\times 10^{-3}$ M Gaucho, 2.0 $\times 10^{-1}$ M Calypso, 1.07M Poncho, and cell death occurred at 30 $\times 10^{-1}$ M Jade, 3.3 $\times 10^{-3}$ M Gaucho, 2.8 $\times 10^{-3}$ M Calypso, and 1.42M Poncho. This study provides the first report of genotoxic and cytotoxic effects in peripheral blood lymphocytes following in vitro exposure to commercial neonicotinoid insecticides.*

Cai, B., Deitch, E.A., Ulloa, L. Novel insights for systemic inflammation in sepsis and haemorrhage. *Mediators of Inflammation* 2010 ID 642462 (2010). *Human clinical studies in 2010 demonstrated a connection between the nAChRs and the immune system. In the process of trying to treat severe inflammatory responses in sepsis and haemorrhage (which are a major cause of death in patients in Critical Care), a specific anatomical and physiological connection was proved between the nicotinic acetylcholine anti-inflammatory receptors in the central nervous system, via the vagus nerve, to the innate immune system. This system protects humans against infection and tissue injury.*

Baldi, I. *et al*. Neurobehavioral effects of long-term exposure to pesticides: results from the 4-year follow-up of the PHYTONER Study. *Occup. Environ. Med* **68**: 108-115 (2011). *The first study to provide prospective data on farmer workers in the Bordeaux area of France (1997-98 and 2001-03) suggested long-term cognitive effects of chronic exposure to pesticides and raised the issue of evolution towards dementia.*

Landrigan, P.J, Benbrook, C.M. Symposium on Opportunities and Initiatives to Pesticides. AAAS 2006 Annual Meeting. *In the US, prenatal and childhood exposure to pesticides have emerged as a significant risk factor for neurodevelopmental disorders, including learning disabilities, dyslexia, mental retardation, attention deficit disorder and autism, which are now affecting 5-10% of 4 million children.*

Brain tumour UK: 40,000 brain tumour patients missing from the official statistics. March 2009 www.braintumouruk.org

Watts, C. Brain Cancer: An Unrecognised Clinical Problem. *Oncology News,* Volume 5 Issue 2 May/June 2010. www.oncologynews.biz *Office of National Statistics figures for the UK showed that the number of children dying from brain tumour in 2007 was 33% higher than in 2001**;** in contrast, child deaths from leukaemia were 39% lower than in 2001. In fact, brain tumours have now replaced leukaemia as the commonest cause of childhood death.*

CHEMTrust Report: Gwynne Lyons and Professor Andrew Watterson. July 2010. A review of the role pesticides play in some cancers: children, farmers and pesticide users at risk? www.chemtrust.org.uk *In a UK study in 2010 pesticide exposure of the foetus was linked to later childhood cancer. In the last 35 years the following have increased; non-Hodgkin's lymphoma has more than doubled; testicular cancer has doubled; breast cancer in women has increased by two thirds and in men has quadrupled; prostate cancer has tripled.*

Evidence that neonicotinoids insecticides are toxic to bees for the EU Ombudsman

All the Registration Documents/Fact Sheets for the individual neonicotinoids state that they are toxic or highly toxic to bees; either acutely, or chronically via pollen and nectar.
http://www.epa.gov/opprd001/factsheets/clothianidin.pdf
http://www.npic.orst.edu/factsheets/imidacloprid.pdf
http://www.apvma.gov.au/publications/gazette/2007/11/gazette_2007-11-06.pdf

Krupke, C.H., Hunt, G. J., Eitzer, B.D., Andino, G., Given, K. Multiple Routes of Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE*, **7**, e29268 (2012).
Abstract: *Populations of honey bees and other pollinators have declined worldwide in recent years. A variety of stressors have been implicated as potential causes, including agricultural pesticides. Neonicotinoid insecticides, which are widely used and highly toxic to honey bees,*

have been found in previous analyses of honey bee pollen and comb material. However, the routes of exposure have remained largely undefined. We used LC/MS-MS to analyze samples of honey bees, pollen stored in the hive and several potential exposure routes associated with plantings of neonicotinoid treated maize. Our results demonstrate that bees are exposed to these compounds and several other agricultural pesticides in several ways throughout the foraging period. During spring, extremely high levels of clothianidin and thiamethoxam were found in planter exhaust material produced during the planting of treated maize seed. We also found neonicotinoids in the soil of each field we sampled, including unplanted fields. Plants visited by foraging bees (dandelions) growing near these fields were found to contain neonicotinoids as well. This indicates deposition of neonicotinoids on the flowers, uptake by the root system, or both. Dead bees collected near hive entrances during the spring sampling period were found to contain clothianidin as well, although whether exposure was oral (consuming pollen) or by contact (soil/planter dust) is unclear. We also detected the insecticide clothianidin in pollen collected by bees and stored in the hive. When maize plants in our field reached anthesis, maize pollen from treated seed was found to contain clothianidin and other pesticides; and honey bees in our study readily collected maize pollen. These findings clarify some of the mechanisms by which honey bees may be exposed to agricultural pesticides throughout the growing season. These results have implications for a wide range of large scale annual cropping systems that utilize neonicotinoid seed treatments.

Whitehorn, P.R., O'Connor, S., Wackers, F.L., Goulson, D. Neonicotinoid Pesticide Reduces Bumble Bee Colony Growth and Queen Production. *Science* 1215025DOI:10.1126/science.1215025

Abstract: *Growing evidence for declines in bee populations has caused great concern due to the valuable ecosystem services they provide. Neonicotinoid insecticides have been implicated in these declines as they occur at trace levels in the nectar and pollen of crop plants. We exposed colonies of the bumble bee Bombus terrestris in the lab to field-realistic levels of the neonicotinoid imidacloprid, then allowed them to develop naturally under field conditions. Treated colonies had a significantly reduced growth rate and suffered an 85% reduction in production of new queens compared to control colonies. Given the scale of use of neonicotinoids, we suggest that they may be having a considerable negative impact on wild bumble bee populations across the developed world.*

Henry, M.M., Beguin, M.M., *et al.*A common pesticide decreases foraging success and survival in honey bees. Science **336** (6079): 348-350. (2012) DOI: 10.1126/science.1215039
Abstract: *Nonlethal exposure of honey bees to thiamethoxam (neonicotinoid systemic pesticide) causes high mortality due to homing failure at levels that could put a colony at risk of collapse. Simulated exposure events on free-ranging foragers labeled with a radio-frequency identification tag suggest that homing is impaired by thiamethoxam intoxication. These experiments offer new insights into the consequences of common neonicotinoid pesticides used worldwide.*

Pesticides Action Network North America (PANNA) on the current State of Science on Bees and Pesticides

http://www.panna.org/sites/default/files/Bees&Pesticides_SOS_FINAL_May2012.pdf

Evidence against glyphosate/Roundup® for the EU Ombudsman

Monsanto's Mission Statement for its Projects in Latin America (website)

"*Monsanto is committed to helping improve lives – especially the lives of farmers in small rural communities around the world*." Pablo Vaquero, Monsanto Latin America South corporate affairs director, said: "*Today, we are helping to change the lives of many individuals in remote and forgotten communities where opportunities are scarce. We are convinced that by helping with training and education, as a company, we are able to add value to people and their communities. Projects have been implemented in 14 provinces in Argentina (Buenos Aires, Santa Fe, Córdoba, La Pampa, San Luis, Santiago del Estero, Entre Ríos, Corrientes, Formosa, Misiones, Salta, Tucumán, Jujuy and Chaco) and one in the Republic of Paraguay. Many farmers and people know about Monsanto Company because of the Roundup Ready trait, which is a trait that gives in-plant tolerance to Roundup® agricultural herbicides. The trait was introduced to the market in 1996 and brought a whole new element to farmers. In 1996, farmers could now plant soybeans, spray the soybeans with Roundup, and poof- the weeds were gone and the soybeans were still as healthy as they were before they sprayed the field."*

In 2010, the physicians from these towns told a different story, one which Monsanto and the authorities had suppressed for a number of years. This is a Report from the 1st National Meeting of Physicians in the Crop-sprayed Towns, Faculty of Medical Sciences, National University of Cordoba, Argentina August 27th & 28th 2010.

INGLES-Report-from-the-1st-National-Meeting-Of-Physicians-In-The Crop-Sprayed-Towns.pdf

Summary of Medical Problems

In the whole area there were increases of cancers, birth defects, reproductive and endocrine disorders. All children's birth defects involving neurosurgical operations (neural tube defects) were treated in one hospital therefore they had complete statistics. Those coming from heavily sprayed areas had a rate of birth defects 70 times greater than those in non-sprayed areas. There were also neurological developmental problems in children less than 1 year of age compared with non-sprayed. Genetic tests showed DNA and genetic damage in those exposed to pesticides, compared with non-exposed.

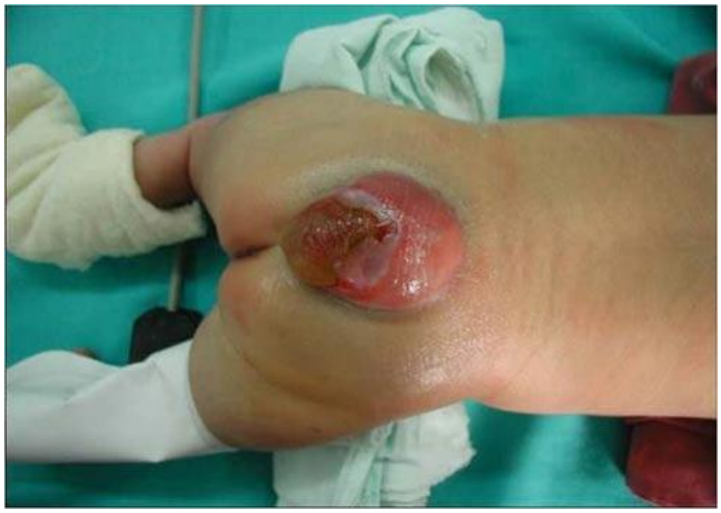
Comparison: heavily sprayed (La Leonesa), with the moderately sprayed (Las Palmas) with the 'not much' sprayed (Puerto Bermejo) towns. The incidence of childhood cancers was three times greater in La Leonesa.

Increased use of pesticides

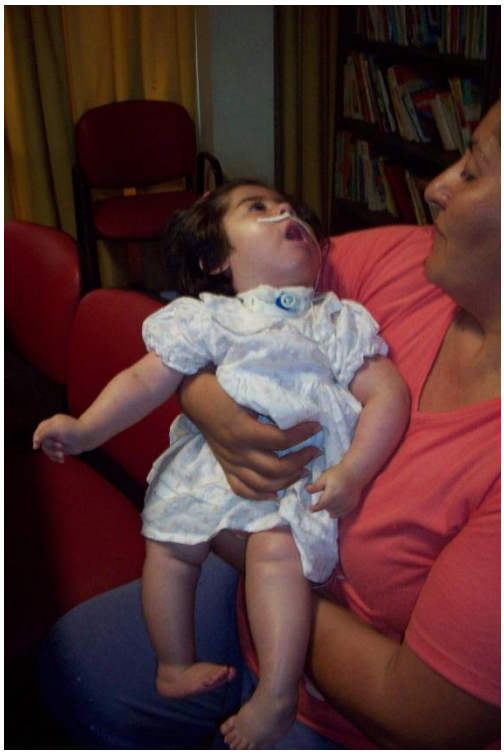
The introduction of transgenic biotechnology Argentina in 1996 accelerated the use of pesticides. 1996: 98 million liters. 2000: 145 million liters. 2009: 292 million liters. 2010: over 300 million liters of herbicides, insecticides, acaricides, defoliants and other poisonous substances.

Glyphosate: 1996: 2 liters/ha. 2009-2010: 10-20 liters/ha, for herbicide-resistant weeds.

Chaco Province RR Soya 1997-2008	1997	2008
	100,000 ha	700,000 ha
Congenital Birth Defects/10,000 live births	15/10,000	82/10,000



A baby with a neural tube defect; this is a meningo-myelocoele. More extensive defects can occur. Hospital de Posadas, Misiones, Argentina. Photograph by kind permission of Dr Graciela Gomez.



Julieta, who died aged 7 months from multiple abnormalities in 2010 Bandera Santiago del Estero Photograph by kind permission of Dr Graciela Gomez

Paganelli, A. Gnazzo, V., Acosta, H., Lo´pez, S L. Carrasco, A.E. Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling. *Chem. Res. Toxic*. 10.1021/tx1001749 (2010).

Abstract: *The broad spectrum herbicide glyphosate is widely used in agriculture worldwide. There has been ongoing controversy regarding the possible adverse effects of glyphosate on the environment and on human health. Reports of neural defects and craniofacial malformations from regions where glyphosate-based herbicides (GBH) are used led us to undertake an embryological approach to explore the effects of low doses of glyphosate in development. Xenopus laeVis embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior-posterior (A-P) axis. Alterations on neural crest markers were later correlated with deformities in the cranial cartilages at tadpole stages. Embryos injected with pure glyphosate showed very similar phenotypes.*

Moreover, GBH produced similar effects in chicken embryos, showing a gradual loss of rhombomere domains, reduction of the optic vesicles, and microcephaly. This suggests that glyphosate itself was responsible for the phenotypes observed, rather than a surfactant or other component of the commercial formulation. A reporter gene assay revealed that GBH treatment increased endogenous retinoic acid (RA) activity in Xenopus embryos and cotreatment with a RA antagonist rescued the teratogenic effects of the GBH. Therefore, we conclude that the phenotypes produced by GBH are mainly a consequence of the increase of endogenous retinoid activity. This is consistent with the decrease of Sonic hedgehog (Shh) signaling from the embryonic dorsal midline, with the inhibition of otx2 expression and with the disruption of cephalic neural crest development. The direct effect of glyphosate on early mechanisms of morphogenesis in vertebrate embryos opens concerns about the clinical findings from human offspring in populations exposed to GBH in agricultural fields.
The broad-spectrum glyphosate based herbicides (GBHs) are widely used in agricultural practice, particularly in association with genetically modified organisms (GMO) engineered to be glyphosate resistant such as soy crops. Considering the wide use of GBH/GMO in agriculture, studies of the possible impacts of GBH on environmental and human health are timely and important.

portal.fagro.edu.uy/phocadownload/taller.../anexo%201%20martinez.pdf

Antoniou, M. *et al.* Roundup and birth defects. Is the public being kept in the dark? (June 2011) *Earth Open Source.*
Extracts: *"The European 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 are found 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. If 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 Roundup and glyphosate in line with the more 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.

Prof Gilles-Eric Séralini and colleagues at CRIIGEN in Caen had already questioned the adequacy of Monsanto's testing both for glyphosate and GM crops.
Séralini, G-E. *et al*. Genetically modified crops safety assessments: present limits and possible improvements *Environmental Sciences Europe* 2011, 2**3**:10 doi:10.1186/2190-4715-23-10. *The 90-day-long tests are insufficient to evaluate chronic toxicity, and the signs highlighted in the kidneys and livers could be the onset of chronic diseases. However, no minimal length for the tests is yet obligatory for any of the GMOs cultivated on a large scale, and this is socially unacceptable in terms of consumer health protection. We are suggesting that the studies should be improved and prolonged, as well as being made compulsory, and that the sexual hormones should be assessed too, and moreover, reproductive and multigenerational studies ought to be conducted too.*

Clair, É., Mesnage, R., Travert, C., Séralini, G-É. A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells *in vitro*, and testosterone decrease at lower levels. *Toxicology in Vitro* **26** (2) 269-279 (2012).
Abstract: *The major herbicide used worldwide, Roundup, is a glyphosate-based pesticide with adjuvants. Glyphosate, its active ingredient in plants and its main metabolite (AMPA) are among the first contaminants of surface waters. Roundup is being used increasingly in particular on genetically modified plants grown for food and feed that contain its residues. Here we tested glyphosate and its formulation on mature rat fresh testicular cells from 1 to 10000 ppm, thus from the range in some human urine and in environment to agricultural levels. We show that from 1 to 48 h of Roundup exposure Leydig cells are damaged. Within 24–48 h this formulation is also toxic on the other cells, mainly by necrosis, by contrast to glyphosate alone which is essentially toxic on Sertoli cells. Later, it also induces apoptosis at higher doses in germ cells and in Sertoli/germ cells co-cultures. At lower non-toxic concentrations of Roundup and glyphosate (1 ppm), the main endocrine disruption is a testosterone decrease by 35%. The pesticide has thus an endocrine impact at very low environmental doses, but only a high contamination appears to provoke an acute rat testicular toxicity. This does not anticipate the chronic toxicity which is insufficiently tested, and only with glyphosate in regulatory tests.*

Marc, J., Bellé, R. Formulated Glyphosate Activates the DNA-Response Checkpoint of the Cell Cycle Leading to the Prevention of G2/M Transition 2004, *Toxicological Sciences:* **82,** (2) 436-442. Robert Bellé's team at Le Centre National de la Recherche Scientifique (CNRS) Roscoff, found that Formulated glyphosate, (Roundup®), activates what is called the checkpoint. Each cell has two checkpoints that are activated only when there are problems in cell division. *"This may reflect interference of the product at the DNA level, potentially leading to genetic instability which is recognized as one the main forces driving the onset and progression of carcinogenesis.*

Gasniera, C. *et al*, Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology doi:10.1016/j.tox.2009.06.006.*
Extracts: *"We exposed human liver HepG2 cells, a well-known model to study xenobiotic toxicity, to four different formulations and to glyphosate, which is usually tested alone in chronic in vivo regulatory studies. We measured cytotoxicity with three assays (Alamar Blue®, MTT, ToxiLight®), plus genotoxicity (comet assay), anti-estrogenic (on ER_, ER_) and anti-androgenic effects (on AR) using gene reporter tests. We also checked androgen to estrogen conversion by aromatase activity and mRNA. All parameters were disrupted at sub-agricultural doses with all formulations within 24 h. Aromatase transcription and activity was disrupted from 10 ppm. Cytotoxic effects started at 10ppm with Alamar Blue assay (the most sensitive), and DNA damages at 5 ppm. A real cell impact of glyphosate-based herbicides residues in food, feed or in the environment has thus to be considered, and their classifications as carcinogens/mutagens/reprotoxics is discussed."*

Modified Bt toxins are not inert on non-target human cells, but in combination with other pesticides may have side effects on humans.

Mesnage R., Clair E., Gress S., Then C., Székács A., Séralini G.-E., 2012, Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide. *Journal of Applied Toxicology* DOI: 10.1002/jat.2712 (2012)
Abstract: *The study of combined effects of pesticides represents a challenge for toxicology. In the case of the new growing generation of genetically modified (GM) plants with stacked*

traits, glyphosate-based herbicides (like Roundup) residues are present in the Roundup-tolerant edible plants (especially corns) and mixed with modified Bt insecticidal toxins that are produced by the GM plants themselves. The potential side effects of these combined pesticides on human cells are investigated in this work. Here we have tested for the very first time Cry1Ab and Cry1Ac Bt toxins (10 ppb to 100 ppm) on the human embryonic kidney cell line 293, as well as their combined actions with Roundup, within 24 h, on three biomarkers of cell death: measurements of mitochondrial succinate dehydrogenase, adenylate kinase release by membrane alterations and caspase 3/7 inductions. Cry1Ab caused cell death from 100 ppm. For Cry1Ac, under such conditions, no effects were detected. The Roundup tested alone from 1 to 20 000 ppm is necrotic and apoptotic from 50 ppm, far below agricultural dilutions (50% lethal concentration 57.5 ppm). The only measured significant combined effect was that Cry1Ab and Cry1Ac reduced caspases 3/7 activations induced by Roundup; this could delay the activation of apoptosis. There was the same tendency for the other markers. In these results, we argue that modified Bt toxins are not inert on nontarget human cells, and that they can present combined side-effects with other residues of pesticides specific to GM plants.

Danish farmers report side effects with GM Soya fed to pigs

A Danish farming newspaper *Effektivt Landbrug* devoted a sizeable part of its 13 April 2012 edition to the discoveries by pig farmer lb Borup Pedersen that GM soy has a damaging effect both on his animals and on his farming profitability. In the previous 2 years, the farm had experienced piglet diarrhoea and 35 sows had died of stomach problems. In the previous 9 months he had had 13 malformed, but live-born, piglets. Another colleague had had similar experiences. In April 2011 Mr Pedersen changed to GM-free soya, without telling his stockman. Within days the stockman noticed that the piglet diarrhoea had stopped. The Danish Centre for Pig Research is beginning a trial later this year on pigs fed with GM Soya versus pigs fed with non-GMO soya.

A deformed piglet; Siamese twins

Photograph by kind permission
of Ib Borup Pedersen

GM scientists and Monsanto claim that GE crops will reduce the amount of pesticides used and increase the yield in order to feed the world. So far, this has proved to be untrue.

Critical Issue Report: Impacts of Genetically Engineered Crops on Pesticide Use in the United States: The First Thirteen Years November 2009. Charles Benbrook
http://www.organic-center.org/science.pest.php?action=view&report_id=159#

Extracts from preface: *"The dramatic increase in the volume of herbicides applied swamps the decrease in insecticide use attributable to GE corn and cotton, making the overall chemical footprint of today's GE crops decidedly negative. The primary cause of the increase is the emergence of herbicide-resistant weeds. Weed control is now widely acknowledged as a serious management problem within GE cropping systems. Farmers and weed scientists across the heartland and cotton belt are now struggling to devise affordable and effective strategies to deal with the resistant weeds emerging in the wake of herbicide-tolerant crops. Herbicides and insecticides are potent environmental toxins. The USDA has been essentially silent on the impacts of GE crops on pesticide use for almost a decade. The vast majority of Glyphosate Resistant weed populations have emerged in Roundup Ready cropping systems since the year 2000."*

In 2009, Doug Gurian-Sherman, senior scientist in the Union of Concerned Scientists (UCS) Food and Environment Program, published 'Failure to Yield'. In the Executive Summary he says: *"This report is the first to evaluate in detail the overall, or aggregate, yield effect of GE after more than 20 years of research and 13 years of commercialisation in the United States. Based on that record, we conclude that GE has done little to increase overall crop yields."*

www.**ucsusa.org**/.../food_and_agriculture/**failure-to-yield**.pdf

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Permanent Peoples' Tribunal against Agrochemical Transnational Corporations held in Bangalore 3-6 December 2011

On 16th November 2011, Pesticides Action Network issued a Press Release: *From 3-6th December 2011, the Permanent Peoples' Tribunal (PPT) will convene in Bangalore, India, to hear cases brought against six multinational agrochemical companies who stand accused of violating human rights by promoting reliance on the sale and use of pesticides known to undermine internationally recognised rights to health, livelihood and life. Known as the 'Big 6', the indicated agrochemical corporations are Monsanto, Dow, BASF, Bayer, Syngenta and DuPont. Collectively, these companies control 74% of the global pesticide market, making the pesticide/agricultural biotechnology industry one of the most consolidated sectors in the world. The World Bank estimates that 355 000 people per year die of unintentional pesticide poisoning. "The aim of taking the Big 6 to the PPT is to give a voice to the otherwise voiceless victims of pesticides around the world who have suffered as a result of the relentless promotion of toxic poisons by these multinational companies."*

During the course of the tribunal, Pesticide Action Network will invite witnesses including scientists, medical doctors, and lawyers, to prove the charges through expert testimony on pesticides, genetic engineering, intellectual property rights, and other subjects germane to the cases at hand. The PPT will also hear testimony from farmers, farm workers, beekeepers, mothers, young people, scientists and consumers from around the world. The defendants will be served and summoned to offer their perspectives and responses.
Also under indictment are the International Monetary Fund, World Bank, and World Trade Organisation; these entities are charged with facilitating corporate concentration of power through their policies and programs. Additionally, the governments of Switzerland, Germany, and the United States – the home nations of six defendant companies – have been indicted for colluding with, and failing to regulate, corporate power.

www.tpp_bangalore3dec2011.pdf