Regulation of genetically modified plants: state-of-art and improvements

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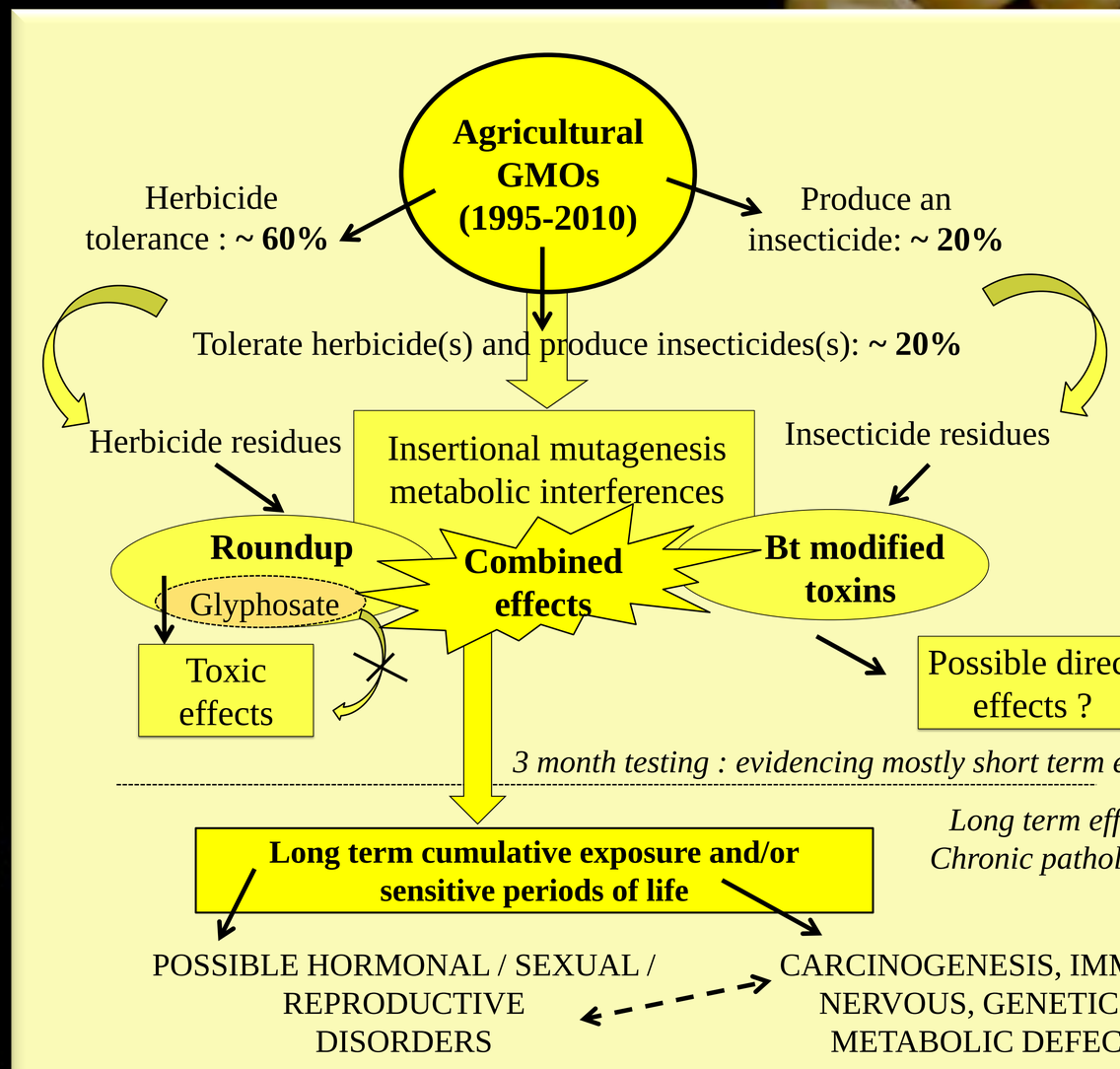

Among the 148 million hectares of genetically modified plants growing worldwide in 2009, more than 99.9 % are described as pesticide plants. Around 80 % are tolerant to Roundup (James, 2011). The latest generation, like Smartstax crops, even cumulate a tolerance up to 2 herbicides and a production of 6 insecticides.

By this widespread use and the known potential hazards of pesticides, their residues are a major concern for health and the environment (Mesnage et al., 2010). In order to highlight potential side effects of GMO consumption, we have reviewed studies of mammals fed with commercialized GMOs from a statistical and a biological point of view.

Meta-analysis of statistical differences with appropriate controls in feeding trials. We reviewed 19 studies of mammals fed with commercialized genetically modified soybean and maize (Séralini et al,. 2011). The data obtained include biochemical blood and urine parameters of mammals eating GMOs with numerous organ weights and histopathology findings. Here we performed a meta-analysis of all the in vivo studies published.

All parameters measured in vivo in GMO toxicity studies	Measured by organ (%) / Total (694-698)		Disturbed in each organ (%) / Total disrupted parameters (~ 9%)	
	Females	Males	Females	Males
Liver	22.9	22.9	**30.8**	26.1
Kidney	23.7	23.7	26.4	**43.5**
Bone Marrow	29.5	29.5	29.7	22.8
Total for 3 tissues	76.1	76.1	86.9	92.4

The different parameters are classified according to the tissue (Séralini et al. 2007) to which they are related (e.g. liver, kidney, bone marrow). 76.1% of the total parameters measured are related to these 3 organs. This metaanalysis revealed that the kidneys were particularly affected, concentrating 43.5% of all disrupted parameters in males, whereas the liver was more specifically disrupted in females (30.8% of all disrupted parameters). Bold values are significantly over the parameters measured per organ.

Signs highlighted in the kidneys and livers of animals could be the onset of chronic diseases. We thus present the scientific reasons for the crucially different biological interpretations and also highlight the shortcomings in the experimental protocols designed by the companies, and accepted by regulatory authorities (Spiroux de Vendomois et al., 2010).

Critical parameters and interpretations	Present regulatory assessment	Improvements proposed	Main consequences if improvements not applied
Number of animals / group	10 measured on 20 /group	At least 20 rats for 3 months, 10 or more for 24 months / group	Low statistical power
Number of controls versus treatments	Too many reference or control groups (320)/ 80 GMO-treated only	Avoid to multiply completely different control groups	Risk of concealing statistical effects
Species	Rat only (in mammals with blood analyses)	Rat and other(s) species such as Mice / Rabbit	Results too much species-specific
Replication of toxicological test	Only once	At least two	Reproducibility, Reliability not proven
Length	Subchronic (3 months)	Chronic (24 months) + developmental + transgenerational	Missing long term, fetal or transgenerational effects
Doses	2 doses	3 doses	Missing dose response relationship
Type of treatment	GMO	GMOs with/without associated pesticides	Confusion between mutagenesis / pesticides effects
Food composition	Substantial equivalence	More detailed composition with specific pesticides residues and metabolites, adjuvants	Missing potential contaminants and combined effects
Norms followed	OECD 408 strictly or less	OECD 408-453 with other details	Lack of hormonal sex specific data for instance
Number of blood analyses	2 measures only after 5 and 14 weeks	At least 3 the first trimester	Missing punctual phenomena
Biological interpretations Dose-effects	"Dose-related": proportional effects only taken into account with two doses !	Non linear effects to be studied (U or J curves)	Risk to avoid endocrine, carcinogenic, immune long-term effects…
Biological interpretations Sex specificity	Effects studied only if occurring in both sexes	Sex specific effects to be studied	Risk to avoid endocrine-specific effects
Biochemical modifications linked to histopathology	Necessary	Not always possible in 3 months	Risk of false negative results
Amplitude of effects studied	Effects inside of undefined historical norm of the species not studied	Any statistical difference with controls to be studied	Risk of false negative results
Final biological conclusion for an effect	Should be plausible for the regulatory committee	Necessity of more objective criteria: ex. lengthening of the test	Major risk of subjective interpretation

Bibliography:

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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.