

The semantics of the term “genetically modified organism”

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Owing to the difficulties in properly delimiting the meaning of the term “genetically modified organism” (GMO), as applicable to transgenic fish, the following critical considerations on EU regulation 1829 concerning the definition of GMO are proposed, in order to better understand the assumptions from which a definition has been enucleated that is now of public use.

Regulation 1829

This Regulation provides uniform procedures throughout the EU for the assessment and authorisation for the use in the EU of GMOs and of feed made from or using GMOs or their derivatives. It also provides for the labelling of such food. Regulation 1829 was made on 22 September 2003. It was published in the official journal on 18 October 2003, came into force on 7 November 2003 and became legally binding with direct effect in the EU from 18 April 2004.

For the purposes of Regulation 1829, GMOs are defined as such within the meaning that has been given to that by Article 2(2) of Directive 2001/18/EC. Excluded from this are organisms obtained through the techniques of genetic modification set out in Annex 1B of that Directive.

That definition of GMOs is set out as follows.

Article 2 – Definitions

For the purposes of this Directive:

- (1) organism means any biological entity capable of replication or transferring genetic material;
- (2) genetically modified organism (GMO) means an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination;

Considerations

In this definition, the term “genetically modified organism” (GMO) is process-based rather than product-based (see above).

The focus of the definition is on the alteration of the genetic material *per se*, that is the genotype, without reference to the changes induced in the phenotype.

The definition allows easy screening of organisms between GMOs and non-GMOs according to the techniques involved.



Phenotypic changes are evaluated only in the risk-assessment phase in the organisms classified as GMOs.

The approval of GMOs for mass production or commercialization is conditioned by a favourable benefit/risk ratio.

The EU definition does not include:

- interspecific hybridization
- transfer of multiple foreign gene by introgressive hybridization;
- inbreeding for pure line formation
- induced polyploidization
- selection of spontaneous mutations
- induced mutations by genotoxic substances or irradiation
- viral transformation

However, there is the possibility of significant risks even with these techniques (*e.g.* generation of killer bees by crossing African and European strains; tetraploidy is a natural fast mode of speciation; mutations can be variably deleterious or harmful; viral vectors may become permanently integrated and vertically transmitted).

On the other hand, the definition would include:

- gene-knockout organisms (lacking a functional gene)
- organisms with DNA encoding anti-sense mRNA (impairing translation of endogenous mRNA)
- organisms subjected to dominant-negative technology (reducing the activity of a protein)
- diploid gynogenetic and androgenetic clones (totally homozygous and with ineffective allele recombination).

It should be emphasized that the threat is not posed by techniques, or by altered genetic information *per se*, but rather by the expression of this information into modified phenotypic traits. The product and not the process is really the source of risk (see above).

The definition should be more comprehensive with the inclusion of all techniques capable of producing significantly modified phenotypes.

On the other hand, the specification of GMO should be considered as a provisional notation, inasmuch as the terms “modification” or “alteration” do not indicate whether the introduced change is risky or not.

The risk assessment phase is, therefore, in charge of defining this aspect. In the case of GMOs for food, the recognition of the safe application of the “substantial equivalence principle”, the lack of foreseeable permanent ecosystemic impacts due to complete reproductive sterility, and obviously the association of some consumer benefits should imply the removal of the labelling as GM and its replacement by a positive notation, such as “genetically approved (GA)”, or a bar-code describing the whole evaluation and approval process. In other words, emphasis should be given to the terminal act of the process (the result of the risk evaluation) rather than the initial act that started the process (the generation of the GMO).



If the GMO production involves the use of less possible environmental and food contaminants, such as pesticides, herbicides, fungicides etc., or the acquisition of substantially better nutritional qualities, then the label should indicate this positive character with the notation “genetically improved” (GI).

The EU definition of GMO does not really specify whether all the genomic copies within an organism must be altered by integration of a foreign sequence or only a few of them. In the first case, DNA-vaccinated organisms would be excluded from GMOs, even if there is a remote risk of somatic genomic integration. Otherwise, somatic gene transfer will be equated to germinal gene transfer and DNA vaccination subjected to the same requirements (e.g. reproductive sterility) as canonical transgenesis.

If DNA-vaccinated fish are not to be considered as GMOs, by the same token, also mosaic transgenics should be excluded. Paradoxically, by *naturally* crossing a mosaic transgenic with a wild-type conspecific, a transgenic line homozygous for the transgene may be obtained by natural mating. These transgenics would not be classifiable as GMOs.

This impasse would be overcome by stating that, in GMOs, the gene transfer must affect the germinal cell line and that this should be functional in order to allow the vertical transmission of the transgene (non-gametogenic germinal cells are equivalent to somatic cells). In this case, fertile transgenics would qualify as GMOs, but totally sterile transgenics would not.

