Assessing the Safety of Genetically Modified Crops

The use of genetically modified (GM) crops is controversial in some parts of the world. In part, this is because of uncertainty about whether the crops are safe to cultivate and consume. Concerns about the safety of GM crops are similar to those about crops produced by new breeding techniques, such as gene editing.

What are GM crops?

Most GM crops contain one or a few new sections of DNA stably inserted into their genome to confer new traits. Various physical and biological methods are available for stably inserting DNA into crops. These include firing small metal pellets coated with DNA into plant cells using a "gene gun" or harnessing bacteria or viruses that transfer their own DNA into plants. The most widely used GM crops are maize, soybean cotton and oilseed rape that have been modified to be herbicide tolerant or insect resistant or both. Many of these crops have been on the market in some countries for over 20 years. Commercialisation of GM crops with improved nutritional qualities has begun over the last five to ten years.

What is safety?

A dictionary definition of safety is the condition of being protected from harm. This definition raises two problems. First, protection from harm when using a product cannot be guaranteed. Second, harm means different things to different people. Controversy about whether GM crops are safe to use often arises because people want certainty that no harm will result, while at the same time being reluctant to define what they mean by harm. Environmental harm is usually more difficult to define than is harm to human and animal health.

We may think of safety as shorthand for "acceptable risk". However, this creates further problems of definition. Not only must we still define harm (risk is a combination of the probability and severity of harm) but also acceptability. We may decide that a risk is acceptable if it is outweighed by the value of potential benefits. This raises questions about who benefits from GM crops and whether the benefits are distributed fairly between producer and consumer. Some regulatory systems for GM crops do not consider potential benefits, which means that acceptable risk is difficult or impossible to demonstrate.

Intended and unintended effects

GM crops have the potential to cause harm through side effects of the intended change or through unintended changes that arise through the process of genetic modification. For example, a crop modified to produce a protein to control insect pests could cause harm because the insect-control protein is toxic to people or to wildlife, or because protecting the crop against insects turns it into a troublesome weed. In theory, harm could also arise if insertion of the DNA coding for the protein disrupted other genes in the crop, perhaps leading to the production of a toxin or allergen. Both types of effect are considered in safety assessments for GM crops.

Assessing the risks from intended effects

Toxicity

All new proteins produced by GM crops are tested for their toxicity to mammals. Testing protocols are similar to those used to assess the dietary toxicity of chemicals. Mice are given large oral doses of the purified novel protein and monitored for adverse effects, such as increased mortality or slower growth relative to controls. Any protein intended to control pests undergoes additional toxicity testing to assess its ecological risks. Species tested include fish, birds and terrestrial and freshwater invertebrates. All toxicity studies aim to expose organisms to doses or concentrations of protein at least 10 times higher than the likely worst-case exposure through the crop. For mammals, the doses may be hundreds or thousands of times higher. Absence of adverse effects in these circumstances is taken to indicate negligible risk from protein toxicity. Depending on their severity, adverse effects may indicate unacceptable risk or the need for further testing under conditions that are more realistic.

Allergenicity

The potential for new proteins to cause allergic reactions is tricky to assess because there is no validated animal test. Instead, a weight-of-evidence approach is used. Proteins that are not similar to known allergens or derived from organisms that produce allergens, are unstable when heated or treated with simulated intestinal fluid, and are unglycosylated, are judged to present low risk of triggering allergic reactions. Decision-making about allergenicity is often precautionary. Regulators tend to be unwilling to conclude that risk is acceptable if one of these conditions is not met.

Ecology

In general, annual crops such as maize and soybeans are not serious weeds of agriculture and do not persist outside cultivation. Nevertheless, risk assessors judge the extent to which the new trait may increase the weediness or invasiveness potential of the crop, often by examining what limits its persistence and spread. Hence, if persistence of a crop is limited by frost, introducing insect resistance is unlikely to cause problems. Increasing drought tolerance, on the other hand, may cause concern, because tolerances to different physical stressors often have common mechanisms. Laboratory or field experiments to check the new crop's ability to survive frost may be prudent in this case. The ecological risks posed by transfer of the genetic modification from the crop to related species by sexual hybridisation are considered in a similar fashion.

Assessing the risks from unintended effects

Risks from unintended effects are assessed by large, multi-location field studies that compare the GM crop with suitable non-GM comparator crops. Compositional analysis studies compare

concentrations of various nutrients, anti-nutrients and toxins, while phenotypic characterisation studies compare the growth and reproduction of the crops. In both cases, statistically significant differences between the GM and non-GM crops are evaluated for "biological relevance". The meaning of biological relevance is problematic. While it is probably intended to mean something like "potentially harmful", it is not defined quantitatively before the studies are conducted. Some argue that prior definition of biological relevance would improve comparative studies. By targeting only characteristics of the plant judged to be important, studies could be better designed and support decision-making more effectively. Others argue that untargeted approaches that make no prior judgement about importance are essential for avoiding wrong decisions and should be extended to cover differences in metabolism and gene expression.

Some regulatory authorities have required feeding studies using grain of the GM crop. These studies have a similar rationale to compositional and phenotypic analysis – screening for unintended differences. The value of feeding studies is controversial on scientific and animal welfare grounds, particularly in the absence of evidence for protein toxicity and important compositional changes in the GM crop.

Conclusions

Assessment of the risks posed by side effects of intended changes in GM crops uses standard principles of toxicology testing. The relevance or completeness of such testing is sometimes disputed. In general, however, regulatory decision-making about the risks from intended effects is relatively straightforward.

Assessment of the risks from unintended effects is more controversial. There is no consensus about the rationale and effectiveness of large studies that compare GM and non-GM crops over multiple characters of undefined importance. Without prior definitions of biological relevance, comparative studies in effect become assessments of the effects of GM as a technique, not the risks posed by particular crops. While it may be important to know the extent to which genetic modification causes unintended changes in crops, there is disagreement about whether this knowledge is a matter for basic research or regulatory risk assessment. Similar controversy will arise about unintended effects of gene editing and other new breeding techniques.

Finally, without greater consensus on definitions of harm, benefit and acceptability, technical advances in risk assessment will do little to reduce controversy about the use of genetic modification and other new techniques in plant breeding.

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