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Expert opinion vs. empirical evidence

The precautionary principle applied to GM crops

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Expert opinion is often sought by government regulatory agencies when there is insufficient empirical evidence to judge the safety implications of a course of action. However, it can be reckless to continue following expert opinion when a preponderance of evidence is amassed that conflicts with this opinion. Factual evidence should always trump opinion in prioritizing the information that is used to guide regulatory policy. Evidence-based medicine has seen a dramatic upturn in recent years spurred by examples where evidence indicated that certain treatments recommended by expert opinions increased death rates. We suggest that scientific evidence should also take priority over expert opinion in the regulation of genetically modified crops (GM). Examples of regulatory data requirements that are not justified based on the mass of evidence are described, and it is suggested that expertise in risk assessment should guide evidence-based regulation of GM crops.

Keywords: evidence-based regulation, expert opinion, risk assessment, precautionary principle, government regulation

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Expert opinion is often sought by government regulatory agencies when there is insufficient empirical evidence to judge the safety implications of a course of action. However, it can be reckless to continue following expert opinion when a preponderance of evidence is amassed that conflicts with this opinion. Factual evidence should always trump opinion in prioritizing the information that is used to guide regulatory policy. Evidence-based medicine has seen a dramatic upturn in recent years spurred by examples where evidence indicated that certain treatments recommended by expert opinions increased death rates.[1] We suggest that scientific evidence should also take priority over expert opinion in the regulation of genetically modified (GM) crops (see **Box 1**). It might be argued that prohibiting or delaying the approval of a (GM) crop based on expert opinion suggesting unreasonable risk (in the face of a weight-of-evidence to the contrary) does not have such dire consequences. However, the delayed introduction of nutritionally enhanced GM crops, such as "golden rice," has been estimated to cause a great many deaths and cases of serious sickness as a result of malnutrition.[2]

Here we discuss two examples where regulation of GM crops based on expert opinion is in conflict with the mass of scientific evidence. The first is the regulatory requirement for crop composition studies (for traits that are not expected to alter plant metabolic pathways). These studies are conducted at great expense (over one million US dollars per study) to investigate whether the insertion of transgenic DNA has unexpectedly caused adverse changes in the composition of the crop. Diverse GM crops, representing well over one hundred GM events, have been tested in such studies without a single case of an adverse effect being detected.[3] Furthermore, transgenesis is consistently characterized by fewer unintended changes compared with traditional breeding, based on the overwhelming scientific evidence on variation in composition among conventional and GM crop varieties.[4]

Combining the findings of lack of adverse changes from unintended effects

Box 1. Why might expert opinion on the risks of GM crops not align with the scientific evidence?

Scientific experts are widely consulted by regulators when assessing risks from using GM crops. Their expertise tends to be in specialist disciplines (e.g., toxicology, entomology, or molecular biology), not in risk assessment. Reliance on specialist scientific knowledge and opinion when devising regulatory guidance can lead to data requirements that are disproportionate to risks.

Specialists often focus on identifying and quantifying potential effects of using GM crops. This misses three important elements of risk assessment and decision-making. First, context is often absent; specialists tend to study effects because they find them scientifically interesting not necessarily because they believe that the effects may lead to harm; this emphasizes the importance of agreeing on definitions of harm at the start of the risk assessment.[17] Moreover, when studying potentially harmful effects of GM crops, the potential for reduced harm compared with the technologies that are being replaced is often not considered. Second, risk assessment should estimate the probability of harmful effects, not simply consider whether they are possible. Finally, precise quantification may be unnecessary for risk assessment; the probability that an effect exceeds a threshold may be sufficient for decision-making.[18]

Reducing scientific uncertainty is often given as reason for requiring specific data for regulatory decision-making concerning GM crops. While reducing uncertainty about an effect may be interesting for a specialist wishing to test a certain hypothesis, this same uncertainty may be irrelevant for assessing safety because the effect is harmless, improbable under conditions of use of the GM crop, or both. Specialists' interests in reducing uncertainty about GM crops for purposes of basic research should not guide data requirements for regulatory risk assessments. Risk assessment is a scientific discipline in its own right and experts in this scientific field should guide the regulation of GM crops.

of transgenesis with our knowledge of how conventional breeding alters crop composition argues against a regulatory requirement for specific studies to assess the composition of each new GM event. For many crops improved through GM technology (e.g., soybean, rice, and maize), not a single conventionally bred variety has been restricted from use based on crop composition over their thousands of years of genetic manipulation and consumption. For other crops, the components known to be compositionally hazardous (e.g., glycoalkaloids in white potatoes) are routinely assessed in new cultivars, irrespective of whether they are GM or not.[4] This empirical evidence appears to be ignored by regulations in favor of 20-year-old precautions[5] as evidenced by the increase in the complexity of some regulatory requirements for compositional studies.[6] In addition to the cost of these trials, lengthy delays in approvals often originate from small but statistically significant compositional differences that have no biological or safety relevance and are expected to occur due to intra-varietal variation when a crop line is derived from a single plant and compared with the composite genetics of the originating cultivar.[7,8] This regulatory requirement becomes even more scientifically untenable in jurisdictions where compositional studies must be repeated when two separate and unrelated GM events, for which compositional safety has been previously demonstrated, are combined through traditional crossing.

A second example, where the preponderance of evidence indicates negligible risk, is the evaluation of potential horizontal transfer of plant transgenes to bacteria. Our expanding knowledge of plant and microbial genomes reveals that transfer of prokaryotic genes to eukaryotes has occurred in an evolutionary time frame, but that the converse (transfer of functional genes from eukaryotes to prokaryotes) appears to have happened rarely, if at all, despite millions of years of opportunity.[9,10] An example of horizontal transfer of a functional gene from a plant to a microbe may eventually be found; however, it is clear from direct evidence that such transfers must be extraordinarily rare.[11] When the negligible potential for gene transfer is coupled with the minimal potential hazard (should transfer actually occur), the overall risk becomes vanishingly small.[12] The regulatory requirement to evaluate the risks of horizontal transfer from plants to bacteria[13] once again seems to distort the intent of the precautionary principle in the face of overwhelming evidence that mechanistic barriers to this type of gene transfer exist.[9]

Other instances of expert opinion leading to regulatory requirements for GM crops that are in conflict with the preponderance of current scientific evidence are not difficult to identify. Examples include studies of the digestive and heat stability of newly expressed proteins to predict allergenic potential, and evaluations of weediness to assess whether highly domesticated crops, such as maize, will become invasive due to the presence of GM traits.[14-16] Evidence-based medicine has been adopted widely to overcome the often erroneous recommendations that can arise from expert opinion. We encourage regulatory authorities to consider this paradigm for the regulation of GM crops so that this technology can be evaluated more efficiently, and when found valuable, more widely applied to address environmental, nutritional, and food-production needs. When scientific evidence is ignored in favor of the expert opinion that shaped some government regulation for GM crops, then the precautionary principal is being distorted to provide spurious scientific rationale for restricting the use of this approach for crop improvement. The implications of regulatory delays for GM crops are often presented in the abstract, such as lost opportunities for innovation; however, the costs are real. Ingo Potrykus put it starkly when discussing delays in approving golden rice: "I...hold the regulation of genetic engineering responsible for the death and blindness of thousands of children and young mothers."[2]

Disclosure of Potential Conflicts of Interest

The authors are employed by companies that develop and market transgenic seed.

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