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How does scientific risk assessment of GM crops fit within the wider risk analysis?

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The debate concerning genetically modified crops illustrates confusion between the role of scientists and that of wider society in regulatory decision making. We identify two fundamental misunderstandings, which, if rectified, would allow progress with confidence. First, scientific risk assessment needs to test well-defined hypotheses, not simply collect data. Second, risk assessments need to be placed in the wider context of risk analysis to enable the wider 'non-scientific' questions to be considered in regulatory decision making. Such integration and understanding is urgently required because the challenges to regulation will escalate as scientific progress advances.

What is the role of scientific risk assessment in the GM debate about?

Scientific risk assessment plays an important part in the regulation of activities that can potentially harm the environment (see Glossary [1]). Many decisions that use the results of scientific risk assessment are controversial: permission to market genetically modified (GM) crops and the control of foot-and-mouth disease are recent notable examples in the UK. In the case of GM crops, scientists have become involved in controversial 'debates' about the validity of the results of scientific research. This seems strange to scientists who think of science as a method for increasing knowledge by objective evaluation of empirical data to test hypotheses, and not as a subject to be put to a vote. In this article we use the example of 'the GM crops debate' to argue that the controversial role of science in setting environmental policy stems from two linked problems. First, scientists have sometimes forgotten that scientific risk assessment, as pure science, should test hypotheses and make predictions from the results of those tests. Collecting data and making vague assertions that they are relevant to risk assessment, without providing specific predictions about things of concern, only serves to confuse and increase unease. A second problem is that the acceptability of a given level of risk cannot be determined scientifically. Scientific assessment of the environmental risks (and benefits) of a technology is not sufficient to set policy and make decisions. Scientific risk assessment must be seen as part of a wider activity that evaluates economic, political, moral and ethical concerns alongside scientific predictions of changes that would result from using the technology. This activity is risk analysis. Hence, part of the GM debate stems from confusions between the collection of data versus

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Glossary

Glossary of terms used in risk analysis, reproduced from the European Commission report on harmonization of risk assessment procedures [1] (http://ec.europa.eu/food/fs/sc/ssc/out84_en.pdf), and from the US EPA ecological risk assessment website (http://www.epa.gov/region5/superfund/ecology/html/glossary.html).

Risk analysis: comprises three components: risk assessment, risk management and risk communication. [We would also include key issue identification as part of the risk analysis.]

Risk assessment: evaluation of risk including the identification of the attendant uncertainties, of the likelihood and severity of an adverse effect(s) or event(s) occurring to man or the environment following exposure under defined conditions to a risk source(s). A risk assessment comprises hazard identification, hazard characterization, exposure assessment and risk characterization.

Stressor: any factor that may harm plants or animals; includes chemical (e.g. metals or organic compounds), physical (e.g. extreme temperatures, fire, storms, flooding, and construction/development) and biological (e.g. disease, parasites, depredation, and competition).

Receptor: the species, population, community or habitat etc that may be exposed to contaminants.

Hazard identification: the identification of a risk source(s) capable of causing adverse effect (s)/event(s) to humans or the environment species, together with a qualitative description of the nature of these effect(s)/event(s).

Hazard characterization: the quantitative or semi-quantitative evaluation of the nature of the adverse health effects to humans and/or the environment following exposure to a risk source(s). This must, where possible, include a dose response assessment.

Exposure assessment: the quantitative or semi-quantitative evaluation of the likely exposure of man and/or the environment to risk sources from one or more media.

Risk characterization: the quantitative or semi-quantitative estimate, including attendant uncertainties, of the probability of occurrence and severity of adverse effect(s)/event(s) in a given population under defined exposure conditions based on hazard identification, hazard characterization and exposure assessment.

Risk management: the process of weighing policy alternatives in the light of the result of a risk assessment and other relevant evaluation and, if required, selecting and implementing appropriate control options (which should, where appropriate, include monitoring/surveillance).

Risk decision: decision-making process involving consideration of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement the optimal decisions and actions for safety from that hazard.

Risk communication: the interactive exchange of information and science-based opinions concerning risk among risk assessors, risk managers, consumers and other actual or potential stakeholders.

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hypothesis-driven risk assessment research, and between risk assessment and risk analysis.

Despite ongoing controversy, it is widely argued that GM crops offer the opportunity for a second 'green revolution', and farmers in North and South America and China, among others, have enthusiastically adopted the first generation of insect resistant and herbicide tolerant GM crops [2]. Economic and health analyses indicate that the crops can be beneficial to both small and large farms [3,4]. However, before GM varieties can be commercially cultivated, compliance with environmental and human health safety assessments is a requirement under international and national legislation. Nevertheless, a heated and highly polarized debate has ensued [5] that has gained great attention not only from those involved and interested in the technology, but also from wider society and the media [5–8]. The use of GM crops in agriculture have been vilified by the media as 'Frankenstein foods' or the producers of 'superweeds' and 'contamination', which has had knock-on effects with supermarkets advertizing the removal of products derived from GM crops and derivatives from their shelves [9–11], public scepticism [5,6,11] and the European Union moratorium [11–13].

Why are we in this position? We identify two possible reasons. The first is the accumulation of data that claim relevance for risk assessment of GM crops, but which answer few questions about risk. These 'answers in search of questions' give the impression of significant risk, whereas relevant studies indicate negligible actual risk. A second reason is the failure to address a set of concerns that currently fall outside the scientific risk assessment; for example fears that agricultural economies will be changed fundamentally by the use of GM crops, leading to undesirable social or political change. Science alone cannot answer these questions, but they should still be addressed. The question is how to integrate these questions into the current analysis of risk.

The relevance of data for environmental risk assessment

Risk assessments (RAs) for GM crops are required by laws that seek to protect or enhance the quality of the environment. Environmental Risk Assessments (ERAs) are used by the US Environmental Protection Agency (USEPA) [14–16], and have great potential for assessing the environmental risks of changes in agricultural practice, including the use of GM crops [17,18]. ERA is considered to be an appropriate way of conducting the environmental aspects of the risk assessment [17,19] The ERA begins after defining the problem: how might the proposed activity, in this case the cultivation of GM crops, affect elements of the environment about which we are concerned? These 'elements' are called assessment endpoints. A conceptual model is developed that links data ('test endpoints') on the hazard and exposure of the crop to predict the risk to the assessment endpoints (Figure 1). Many of the people who are involved in assessing risks of GMOs are geneticists, ecologists, plant scientists, toxicologists, or other experts with in-depth knowledge of relevance to one or

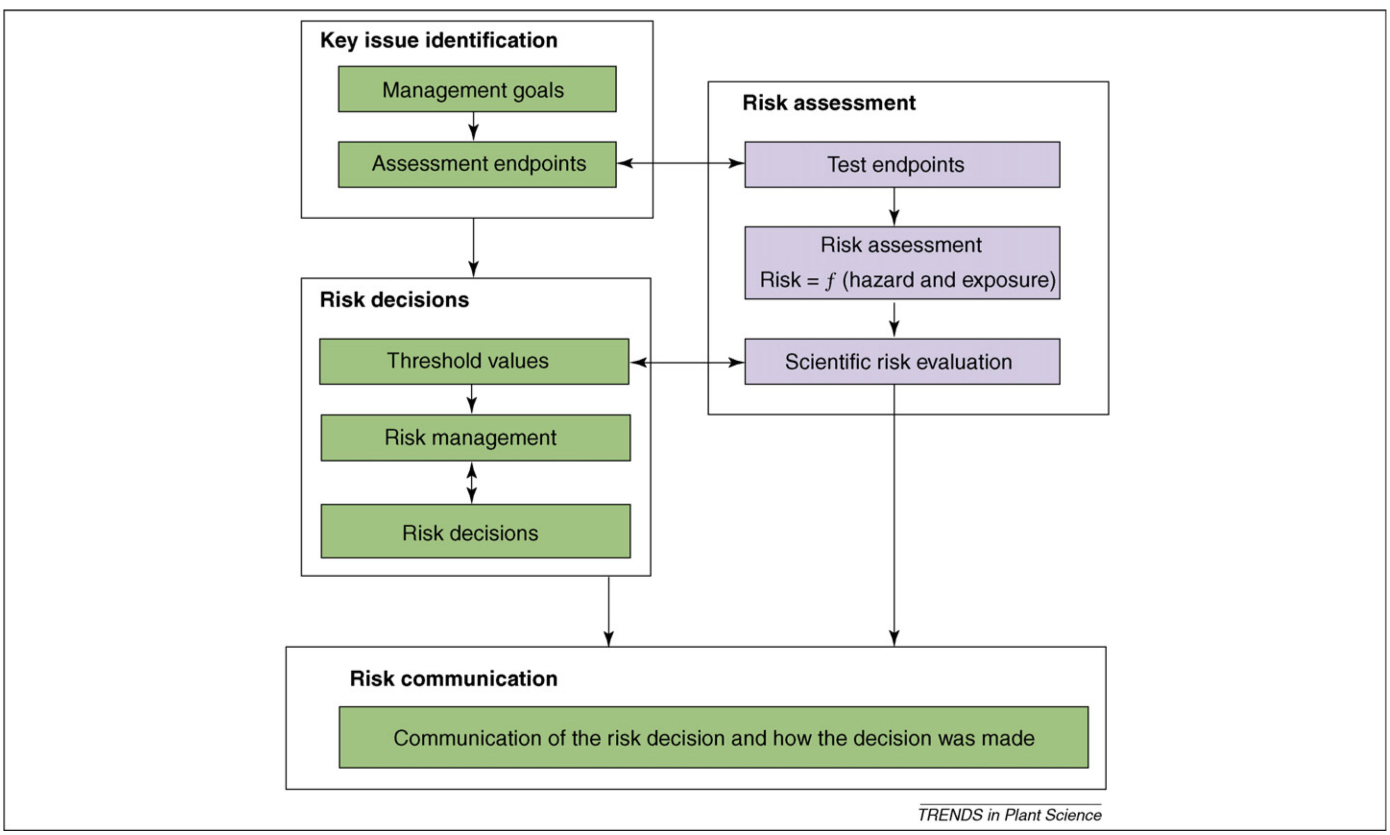

Figure 1. Risk analysis. The diagram depicts the four stages of risk analysis: key issue identification, risk assessment, risk decision-making and risk communication. Boxes highlighted in green are stages driven by society and those highlighted in purple are driven by science. Progression through the system is not linear, but iterative. Feedback loops, although not included in this diagram, are an integral part of risk evaluation.

Box 1. Examples from the literature where hazard has been considered without being placed in the context of exposure or vice versa

H x E

An example of questionable relevance of data is work done on the breeding system and life cycle of oilseed rape in the 1990s in relation to the potential risks of gene flow from transgenic oilseed rape. Many variables were measured, including pollen dispersal distance, the mechanism of pollen dispersal, the longevity of pollen, and pollen tube growth rate. The data appeared relevant – the variables relate to oilseed rape pollen, and pollen effects gene flow – but no theory links these variables to an estimate of gene flow, and the relevance of the data for risk assessment remains obscure [22,23].

A further problem is that even if estimates of gene flow were made, they would only comprise an estimate of exposure. However, an exposure estimate in the absence of other components necessary for risk assessment can create the impression that risk has been demonstrated. For example, Lidia Watrud and colleagues [24] described the detection of gene flow from GM herbicide-tolerant *Agrostis stolonifera* (creeping bentgrass) up to 21 km from the field trial as contributing 'significantly to the ongoing discussion about potential risks of gene flow from GM crops and [our findings] are thus anticipated to be of interest to plant scientists, evolutionary biologists, ecologists, policy makers and regulators'. It is not surprising that a wind pollinated, and largely self-incompatible, perennial species shows long-distance gene flow, and previous studies with non-GM *Agrostis* species have inferred long-distance gene flow from allele frequency data [25]. So the paper merely confirms, albeit elegantly, that there is potential for widespread exposure to transgenes carried by *A. stolonifera*. Even if one accepts that the paper indicates unexpectedly high amounts of gene flow, without a characterization of hazard the paper contributes little to the evaluation of risks; if there is no hazard, there is no risk regardless of how high the exposure. Nevertheless the paper gives the impression that the results are an important step in the assessment of the risks of (not exposure to) GM crops, and that the risks are higher than thought previously.

H x E

Similar criticisms apply to studies of hazard without any exposure data. For example, John Losey and colleagues [26] showed that maize pollen expressing a protein toxic to Lepidoptera was harmful to monarch butterflies; on reflection, an observation as surprising as long-distance gene flow in *Agrostis*. The exposure in the experiment was not quantified, nor was there evidence that there was exposure in the field. Nevertheless, many commentators presented the paper as an indication of the high risk of *Bt* maize to monarch butterflies. Subsequent characterization of exposure of monarch butterfly larvae to maize pollen indicated that the likelihood of harm to monarch butterfly populations was low [4,27,28].

more aspects of risk assessment. A common understanding of the conceptual framework for risk assessment is important so that these various experts and other stakeholders can work together effectively [20]. These data might exist already or be obtained by new studies. The important point is that data are obtained to test specific hypotheses about the amount of risk to the assessment endpoints posed by a stressor. Too frequently, scientific studies were, and still are, being undertaken without a view as to how they will help to quantify risk: either there is no conceptual or theoretical model to link the data and the assessment endpoints or, worse, no assessment endpoints are defined.

When scientific design studies about potential risks are undertaken that have not based their research on definable endpoints – they often measure only one component of the risk estimation. They either set out to unearth potential intrinsic hazards associated with the stressor, or they focus on the potential for exposure to some component of the GM plant without demonstrating whether the component is hazardous (Box 1). There are many examples in the literature where this has occurred, usually leading to considerable confusion and concern. For risk to be properly assessed, both components, hazard (H) and exposure (E), need to be quantified, if greater focus is on one then the risk assessment loses quantitative power [21].

Examples discussed in Box 1 [22–28] of where hazard has been considered without being placed in the context of exposure and vice versa show the importance of a proper discussion of the relevance of results. Studies of hazard or exposure, much less some component of these parameters, should not be presented as characterizing risk. Moreover, for risk to be characterized the data must relate to the effects on specified assessment endpoints; potential effects on things of no concern are, by definition, not risks. If data claim to assess risk, but do not, they merely increase unease about the environmental effects of GM crops, and increase rather than decrease uncertainty. This is one-half of the problems associated with assessing risk, and fuels confusion about risk assessment of GM crops and the wider debate about genetic modification.

Risk assessment and risk analysis

GM crops today in Europe are subject to intense scrutiny [12,29], and European regulations to assess and address the safety of GM crops with regards to human health and the environment are perhaps the most stringent in the world [29,30]. However the stringent regulation has not managed to dispel concerns over the safety of GM crops.

For a regulatory system to be successful it must inspire confidence [31–33]. Much regulation involves the evaluation of technical information by specialists, therefore, for non-specialists there needs to be a strong element of trust, not only in the regulations, but also in the people in charge [6–8,32,34,35].

Numerous criticisms have been levelled at the current regulations [11,31,33–35], including their independence, appropriateness for use in making decisions about applications, the scope of the risks assessed, and the validity of the science that assesses those risks [7,11,29,33,36]. Opponents of the current regulations have proposed solutions. Most involve a broadening of the regulation to encompass a more holistic approach in assessing and addressing risks, so that not only human and environmental safety are evaluated, but also ethical and economic concerns. There are also often calls for the widening of expert panels to include non-expert members to the committees who evaluate applications and advice on decisions for commercial release [8,31,35]. Are these concerns a valid criticism of scientific risk assessment? Our view is that the concerns are legitimate but are not a valid criticism of scientific risk assessment. Scientific risk assessment is just one part of a larger evaluation of the desirability of permitting the cultivation of GM crops, or any other activity judged to raise potential risks. This evaluation is risk analysis and it is here that society's concerns can be addressed. Risk analysis is illustrated in Figure 1.

Risk analysis addresses societal concerns in several ways. First, the specification of management goals in legislation reflects societal concerns. Specific assessment endpoints, such as the populations or habitats of rare species, are also reflections of what society considers important. Another area where societal concerns are incorporated is decision making. The result of the scientific risk assessment is not the decision whether or not to permit the cultivation of a GM crop; it is not even the only factor on which a decision is made. A decision will be made based on the amount of risk that is acceptable (the threshold value) if the crop is permitted to be cultivated, and, just as importantly, the risks of not permitting cultivation. Acceptable risk cannot be determined purely scientifically: science can predict the likelihood of certain effects, but non-scientific criteria must be included in the process of judging their acceptability.

Although the evaluation of risk is a daily occurrence in an ever more risk-averse society, there is often confusion between risk assessment and risk analysis. Risk assessment needs to be scientific to enable the quantification of risk. For example one would not want anyone other then an aeronautical engineer to evaluate whether a plane was safe to fly, so why should it be any different for GM crops? However, although aeroplane safety (risk assessment) should be in the hands of the aeronautical engineers, a consideration of the wider environmental and social impact of increased air travel (risk analysis) should involve a wide range of experts and stakeholders. Thus, the wider societal considerations of relevance to GM crops, including, but not limited to, politics and economics, should play a role in driving the wider risk analysis, from the production of management goals and threshold values to the communication of the risk decision. Not understanding the difference between risk assessment and risk analysis comprises the other half of the confusion about the risks of GM crops within the wider debate about genetic modification.

Taking the heat out of the debate

What can be done to make the debate about genetic modification more measured and less vitriolic? First, scientists have a duty not to present data in a way that implies that risk has been demonstrated, when all that has been done is that hazard or exposure, or some component of these parameters, has been studied. It is irresponsible to claim that work has relevance to risk assessment without explaining how. A minimum requirement should be a conceptual model that links the data to a possible effect on something of value (an assessment endpoint).

Second, all parties in the GM crop debate should be made aware that scientific risk assessment is one part of risk analysis; it is risk analysis that is used to make decisions and that reflects rational non-scientific concerns. Of course, decisions based on scientific and non-scientific arguments are not easy. One possible answer is to reformulate concerns that appear non-scientific into forms that are amenable to scientific analysis. In other words, can we derive assessment endpoints for questions that currently lie outside scientific risk assessment?

The GM crop debate has exemplified how both scientists and members of society can misunderstand their roles as well as those of scientific risk assessment and risk analysis. The result of these misconceptions has been the persistent outrage that has enveloped the GM crop debate in Europe over the past decade [10,20,22]. From this there has been a larger breakdown in society's trust of both scientific applications and the regulatory process safeguarding people and the environment against potential risks. This breakdown in trust could have much more far-reaching consequences for science and the acceptance of other emerging scientific innovation such as future advances in medicine (e.g. stem cell therapy), technological solutions to climate change and nanotechnology. Sustainable development in its widest sense can only be achieved if our innovations are developed in the context of communication, accountability and trust.

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