

Guest Editorial

Conceptualizing risk assessment methodology for genetically modified organisms

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Risk assessment methodology for genetically modified organisms (GMOs) has evolved over the last several years. At a conceptual level, the methodology has been adapted from the existing paradigm for environmental risk assessment, which was developed for chemicals and other types of environmental stressors since at least the 1980s (see Hill and Sendashonga (2003) for discussion).

Many of the people who are or will be involved in assessing risks of GMOs are geneticists, ecologists, plant scientists, toxicologists, or other experts with in-depth knowledge of relevance to one or more aspects of risk assessment. A common understanding of the conceptual framework for risk assessment is important so that these various experts and other actors can work together effectively. Furthermore, a common conceptual framework allows all of the various components of risk assessment to be appropriately organized and brought together in a way that supports decision-making regarding the use, release and/or import of GMOs.

Unfortunately, common understanding regarding the conceptual basis for risk assessment is a challenge. There is considerable variation among risk assessment frameworks for GMOs regarding the steps or components of risk assessment, as well as terminology (SCBD, 2005). There is no need, nor is it possible, to standardize so that everyone agrees on the number of steps in risk assessment and the associated terminology. It is important, however, that when one person refers to a particular component of risk assessment, using a particular term, others can relate that step and that term to whatever framework they use.

Here, I attempt to dissolve some of the misunderstanding by illustrating some of the core elements that are common to many frameworks for risk assessment methodology, and by pointing out two common sources of confusion. Figure 1 aims to show some of the most commonly delineated steps and associated terminology used

in risk assessment frameworks. Somewhat similar versions of this figure can be found in some of the frameworks reviewed in SCBD (2005), such as those from the U.S. Environmental Protection Agency (USEPA, 1998) and the European Union (EU, 2002). Not all of the steps shown in Figure 1 are found in all frameworks. The first step (hazard identification) is considered in some frameworks as a separate initial process (or part of such a process) that precedes risk assessment entirely. In addition, the fifth step (mitigation options) is also not universal among frameworks, as most frameworks clearly separate risk assessment from risk management. Some frameworks, however, consider only certain aspects of risk management (*e.g.*, monitoring) as separate from risk assessment but other aspects of risk management (*e.g.*, consideration of risk mitigation options) to be part of risk assessment methodology, since a final characterization of risks must take into account the effects of any mitigation options that reduce risks. The important aspect is, of course, the iterative and inter-linked relationship between risk assessment and risk management.

Even when frameworks delineate the components of risk assessment in similar ways, there is considerable variation in terminology used to describe each component (Fig. 1). Furthermore, there is also additional terminology confusion when risk assessment is considered in a broader context, including its relationship to risk management and decision-making. For example, the entire process of risk assessment, combined with risk management (and risk communication in some cases), is sometimes referred to as *risk analysis*. This is the case for a few international bodies and standards. In addition, some frameworks consider risk management to encompass decision-making, while others consider decision-making as separate (in the latter case, risk management has a narrower scope).

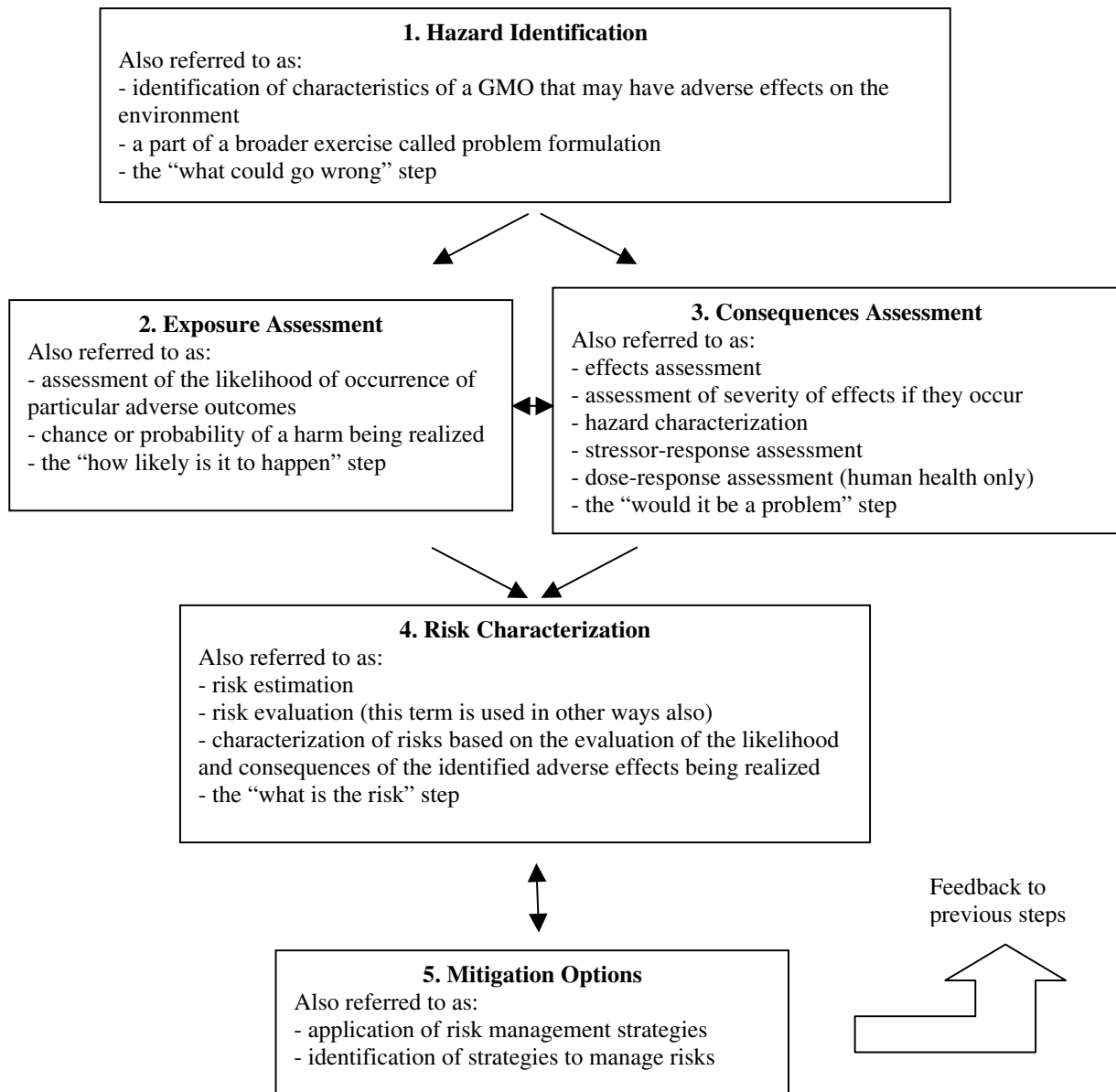


Figure 1. Variation in terminology used to describe methodological components common to many (but not all) risk assessment frameworks. See text for discussion.

However, there is at least one near-universal agreement among risk assessment frameworks – risk as a concept has two components, one related to the possibility of bad thing(s) happening, and the other related to the consequences if those bad thing(s) happen. These two components of risk are conceptually separate. Risk is characterized or estimated, for any particular endpoint, by combining these two components. Thus,

components 2, 3 and 4 in Figure 1 are central to risk assessment and are part of virtually all risk assessment frameworks, either implicitly or explicitly.

Despite widespread agreement on this aspect of risk assessment methodology, there are at least a couple of common misunderstandings that are important to recognize. First, hazard identification (step 1 in Fig. 1) is not the same as the consequences assessment (step 3).

Table 1. Conceptual relationship between the core components of risk assessment. Risks are shown as a function of exposure and consequences. Actual values shown are arbitrary and approximate – a more detailed example of this type of matrix approach can be found in the Australian Risk Analysis Framework (OGTR, 2005). See text for discussion.

| Exposure | Consequences if Exposure Occurs | | | |
|-------------------------------------------|---------------------------------|-----------------|---------------|---------------|
| | Negligible | Minor | Moderate | Major |
| Low likelihood or degree of exposure | Negligible risk | Negligible risk | Low risk | Moderate risk |
| Moderate likelihood or degree of exposure | Negligible risk | Low risk | Moderate risk | High risk |
| High likelihood or degree of exposure | Low risk | Moderate risk | High risk | High risk |

The former is about identifying potential hazards, based on plausible mechanisms by which exposure could occur and lead to adverse effects. Once one or more hazards are identified, the assessment considers both real-life exposure, and the potential consequences that would be associated with exposure (or a range of possible exposures if there is uncertainty) if exposure occurs. Some confusion arises because of the occasional use of the word “hazard” in both steps 1 and 3 in Figure 1. For example, the Codex Alimentarius Commission uses the terms hazard identification and hazard characterization to refer to these steps (Codex, 2003). Similarly, the formula “risk = hazard times exposure” found in some literature exacerbates this misunderstanding by associating the word hazard with the consequences assessment (3). This misunderstanding is avoided by most frameworks because they reserve the word “hazard” for use only in step 1 (hazard identification) in Figure 1, and do not use it at all for step 3. While the formula “risk = hazard times exposure” works fine for those who use and understand it, care must be taken to clarify the nature of the “hazard” component, in particular to ensure that it is not confused with the initial step of hazard identification.

Why is this important? The distinction between hazard identification and all other steps is critical. Failure to distinguish hazard identification usually means that it is glossed over, yet this important first step is what allows the assessor to scope out the problem and to determine what to assess and at what level of detail. There may be several types of potential hazards associated with a GMO, and it is important to clarify conceptually the pathway or mechanism for each. Without this initial step, risk assessment can be much less focused and may not account for all possible hazards. For example, in the case of toxic effects of *Bt* maize on monarch butterflies, a proper hazard identification might consider whether the endpoint of interest is mortality of individual butterflies, mortality rate for an entire monarch population, and/or viability of a predator population that depends on the monarch population. Without this kind of scoping as part of hazard identification, it will be unclear what data must

be used or gathered to support the exposure assessment (2) and the consequences assessment (3). If hazard identification is done rigorously, it may involve a very preliminary consideration of exposure and consequences based on existing data and conservative assumptions, with the aim of determining if a detailed risk assessment involving collection of new data is warranted. Whether the assessor refers to this initial step as hazard identification, problem formulation, or even a “scoping-level” or “tier-1” risk assessment, is unimportant – the key principle is that there is a rational, iterative process for determining whether to conduct a detailed assessment and exactly what the assessment should entail in order to support decision-making regarding use, release or import of a GMO as the case may be.

A second common misunderstanding regarding risk assessment is that consequences assessment (3) and risk characterization (4) are the same step, or two parts of the same step. This is not the case. The consequences assessment is an assessment of consequences *if* exposure occurs. Risk characterization (4) combines exposure assessment (2) and consequences assessment (3) – Table 1 illustrates the interaction between steps 2 to 4 in risk assessment. This conceptual framework applies regardless of whether the assessment is qualitative or quantitative. Distinguishing among these three steps is crucial. The famous study by Losey et al. (1999) assessed the consequences to individual monarch butterflies of exposure to pollen from *Bt* maize. This study did not specify exposure levels exactly, and thus its main value was in identifying a potential hazard (1), but it also showed qualitatively that there were consequences associated with exposure (3). Most people recognized this study for its value in identifying a potential hazard. Some, however, without any information on potential real life exposure compared to exposures in the lab study, let alone extrapolation from individual to population-level effects, reacted by assuming that there was a real risk to monarch butterfly populations associated with use of *Bt* maize. The subsequent formal assessment of this risk pathway by Sears et al. (2001) showed that the risks

were low, mainly because the percentage of the monarch population exposed to the *Bt* toxin was very low.

The same conceptual framework to assessing risk applies not only to toxic effects on non-target organisms, but also to other mechanisms of risk. For example, one potential hazard that may be identified with a transgenic crop is transfer of herbicide tolerance to agricultural weeds. In this case, the exposure assessment might focus on gene flow and introgression, by asking how likely are gene flow and introgression to occur and to what extent. The consequences assessment might focus on asking how severe the consequences would be if the weed species possessed the trait for herbicide tolerance. If there is uncertainty about gene flow and introgression, the consequences assessment (3) might involve determining the relationship between varying levels of gene flow/introgression and the associated severity of consequences. The risk characterization occurs by combining that relationship with the actual exposure estimation (2).

It is important to note that in the example of gene flow above, estimation of gene flow itself is associated with the exposure step of risk assessment. Estimation of gene flow *per se* is not generally considered to be a complete risk assessment, unless one considers the presence of a transgene to be an adverse effect (*i.e.*, “contamination”). Risk assessment requires not only an evaluation of exposure, but also an evaluation of some potential adverse consequence(s) (step 3). Assessments that focus only on gene flow yet attempt to draw conclusions about risk, are implicitly assuming that there will be consequences resulting from gene flow, or are implicitly expressing the view that gene flow itself is an adverse consequence. Such assumptions and value judgments should be made explicit. Even a very simple consideration of potential consequences that could result from gene flow is better than none at all. A proper hazard identification (step 1) should lay out the exact mechanism(s) by which gene flow may lead to adverse effects, and any plausible hazards identified would be identified on the basis of some understanding about potential consequences.

Biosafety experts may not feel a need to step back and examine the conceptual basis for risk assessment. After all, gene flow experts already know how to study gene flow, toxicologists already know how to study effects of

Bt genes on monarch butterflies, and entomologists already know how to estimate resistance risks. However, looking at all of these different types of risks together in a single, integrated assessment that is understandable and useful to decision-makers is not so easy. Common understanding of risk assessment methods at a conceptual level is therefore critical in this regard.

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