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Protection goals in environmental risk assessment: a practical approach

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Abstract Policy protection goals are set up in most countries to minimise harm to the environment, humans and animals caused by human activities. Decisions on whether to approve new agricultural products, like pesticides or genetically modified (GM) crops, take into account these policy protection goals. To support decision-making, applications for approval of commercial uses of GM crops usually comprise an environmental risk assessment (ERA). These risk assessments are analytical tools, based on science, that follow a conceptual model that includes a problem formulation step where policy protection goals are considered. However, in most countries, risk assessors face major problems in that policy protection goals set in the legislation are stated in very broad terms and are too ambiguous to be directly applicable in ERAs. This means that risk assessors often have to interpret policy protection goals without clear guidance on what effects would be considered harmful. In this paper we propose a practical approach that may help risk assessors to translate policy protection goals into unambiguous (i.e., operational) protection goals and to establish relevant assessment endpoints and risk hypotheses that can be used in ERAs. Examples are provided to show how this approach can be applied to two areas of environmental concern relevant to the ERAs of GM crops.

Keywords Environmental risk assessment · Genetically modified crops · Protection goals · Assessment endpoints · Policy · Regulation

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Introduction

Environmental risk assessments (ERAs) are an essential part of regulatory decision-making for genetically modified (GM) crops in most countries. These risk assessments are analytical tools, based on science, which help decision making. To conduct useful ERAs, it is essential that environmental policy protection goals are considered. Ideally, the environmental resources to be protected, the degree of protection they deserve, or the maximum impacts that should be tolerated, will be set by policy before ERAs are conducted. However, in most countries, policy protection goals set in the legislation are stated very broadly and are too ambiguous to be directly applicable in ERAs. In addition, in most countries, not only are clear definitions of what needs to be protected missing, but there are no definitions of what effects of a GM crop would be considered as harmful to the environment. This means that risk assessors have to interpret policy protection goals without clear

guidance on what effects would be considered harmful. In some countries, this problem is proving difficult to solve: changes in environmental policy or specification of levels that would constitute environmental harm may not be a priority. Meanwhile ERAs to support regulatory applications for the approval of GM crops have to continue. In this paper we propose a practical approach that may help risk assessors to translate policy protection goals into unambiguous (i.e., operational) protection goals that can be used in ERAs. The formulation of operational protection goals in turn helps the identification of assessment and measurement endpoints.

Operational protection goals

In general, policy protection goals are designed to be broad so they can be easily agreed at political level (Evans et al. 2006). Another advantage of breadth is that protection goals do not have to be continually redrafted to cope with new situations and scientific developments. Hence legal definitions of protection goals use broad normative concepts such as "sustainability", "integrity" and "acceptability". These concepts, unless clearly defined, can be interpreted in many different ways and they become almost impossible to predict or to measure objectively. Different groups may have different interpretations of what is sustainable or what is acceptable. Ideally, therefore, these policy protection goals should be translated into operational protection goals in the regulatory framework so that ERAs can focus on the key concerns for decision-making. As discussed above, this is not often the case, so it falls to the risk assessors to interpret the policy objectives and turn them into operational protection goals.

In most countries, despite a clear will to protect the environment, environmental policy protection goals are not always clearly defined. Nevertheless, the protection of biodiversity and sustainable agricultural production are almost universal protection goals. ERAs for GM crops aim to support these policy protection goals. Several areas of assessment are usually considered, such as persistence and invasiveness of the GM crop, its effects on non-target organisms, its effects on soil, and so on. Protection of biodiversity and protection of agricultural production can sometimes appear to be in conflict. In the case of herbicide tolerant crops, which have been introduced to improve management of weeds, there has been much discussion regarding the potential benefits to agriculture and the potential adverse effects on biodiversity from changes in the abundance or types of weed. These conflicts are often found during the ERA, and in the absence of clear policy guidance, all the risk assessor can do is to highlight the effects of using the product, and that the effects may be beneficial, adverse or neutral depending on which protection goal is considered. It is then the task of risk managers to make a decision by weighing the risk against the potential benefit.

One way to translate policy protection goals into operational protection goals for ERAs of GM crops is to use an ecosystem services approach. This approach has been proposed for adoption in other regulatory frameworks, such as the plant protection product registration in the EU (Nienstedt et al. 2012). Other conceptual frameworks are available for making policy objectives operational; for example, natural resource management (e.g., Keough and Blahna 2006). Like ecosystem services, these methods seek ways to balance economic, social and environmental objectives. We discuss the ecosystem services concept as a means of illustrating the process of making policy objectives operational. We do not necessarily advocate it as the only or best method in all circumstances.

The ecosystem services concept was first formally described in the Millennium Ecosystem Assessment (MEA) (MEA 2005). The ecosystem services approach takes into consideration the benefits that humans receive from particular ecosystems. They comprise provisioning services (e.g. food production), regulating services (e.g. biological control or pollination), cultural services (e.g. recreation, cultural heritage) and supporting services (e.g. nutrient cycling) (Nienstedt et al. 2012). Different types of ecosystems will therefore offer different types of ecosystem services. Usually not all services can be protected at the same level and conflicts often arise requiring trade-offs to be made.

Using the ecosystem services approach, the most relevant services can be identified in order to establish the desired level of protection. In an agricultural context, the most relevant ecosystem services will vary depending on the spatial scale considered. In cropped areas, one of the most important services is the production of food. This provisioning service is supported by regulating services, such pollination and pest regulation, and supporting services, such as

decomposition of organic matter, soil nutrient cycling and water regulation and purification (Sanvido et al. 2012; Moonen and Barberi 2008). Cultural services from cropped areas may also be considered. For example, in heavily urbanized countries, like the UK, crops are considered important habitats for valued farmland bird species, which, among other things, provide a recreational service to birdwatchers (Tscharntke et al. 2012). Using this approach, policy protection goals can be translated into operational protection goals that focus the objectives of protection on valued ecosystem services in the agricultural context.

ERAs for GM crops typically consider a range of areas of assessment: (1) persistence and invasiveness of the crop, (2) effects on non-target organisms, (3) effects on soil (e.g. Devos et al. 2013; Raybould et al. 2010). Some countries specify additional areas of assessment in their regulations. For each area of assessment, specific operational protection goals can be defined. Ideally, these protection goals should be defined by policymakers, because this would ensure consistency among regulatory submissions as they would be based on the same set of operational protection goals. However, in most countries this is not the case. Risk assessors face having to formulate operational protection goals based on their interpretation of policy protection goals and what they consider relevant about the product under assessment. In these cases, an open dialogue between the scientists conducting the risk assessment and the risk managers making decisions is crucial so that key operational protection goals can be agreed before the assessment begins. This will increase the value of the ERA by providing the information necessary for decision making.

Formulating assessment endpoints, risk hypothesis and measurement endpoints

Once the operational protection goals for each area of assessment are defined, assessment endpoints associated with a particular goal can be formulated: *"Assessment endpoints are specific entities and their attributes that are at risk and that are expressions of a management goal"* (USEPA 2003). Not all valued organisms or ecosystem features can be studied, therefore assessment endpoints are carefully selected usually based on ecological relevance, susceptibility (likely exposure plus likely sensitivity), and relevance to policy protection goals. Selecting appropriate assessment endpoints is a critical step in ensuring that an ERA will be useful to risk managers in making informed and scientifically defensible environmental decisions.

Assessment endpoints are identified during the problem formulation phase of environmental risk assessment (Gray 2012; Raybould 2006; Wolt et al. 2010). This process is well described by Sanvido et al. (2012) and Nienstedt et al. (2012). Specific assessment endpoints comprise the following components:

(a) The entity to be protected (e.g., non-target arthropods species or functional groups)
(b) The attributes or functions of those entities to be protected (abundance, function).
(c) The unit of protection (individuals, populations, function)
(d) A spatial unit of protection (such as ''GM crop fields'', ''other arable land'', and ''non-agricultural habitats'').
(e) A temporal scale of protection (such as the present cropping season, the following cropping season, or the time approved for cultivation of the GM crop).

Sometimes, the definition of an assessment endpoint includes definitions of adverse effects, such as the direction or size of change to the specified attributes.

There could be several assessment endpoints associated with one operational protection goal. The number will be determined during problem formulation where the ecological entities to be protected will be identified.

It is important to remember that assessment endpoints are not the same as measurement endpoints. While assessment endpoints define what is going to be assessed to determine the probability that an adverse effect relating to the protection goal will occur, measurement endpoints are the results of studies that test hypotheses about the effects on an assessment endpoint of exposure to a stressor (Fig. 1). Assessment endpoints are, therefore, evaluated but not necessarily measured during the risk assessment.

Examples

To illustrate the proposed process for translating policy protection goals into operational protection

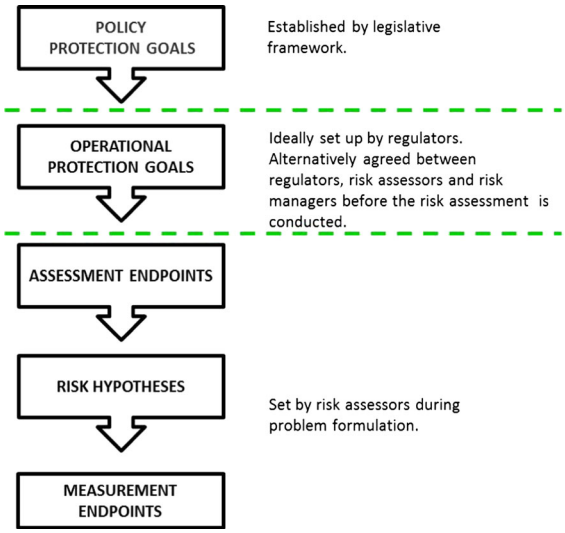

Fig. 1 Proposed process for translating policy protection goals into operational protection goals, assessment endpoints and measurement endpoints to use in environmental risk assessment

goals two examples are given below. The examples represent two of the assessment areas that are commonly considered in ERAs to support applications for the cultivation of GM crops in most regulatory frameworks around the world: persistence and invasiveness and effects on non-target organisms.

Persistence and invasiveness

One feature that is often considered in ERAs for GM crops is the persistence and invasiveness of the crop, which in some regulatory systems is referred to as its "weediness potential". The concern is that the genetic modification may have changed the phenotype of the crop making it more "weedy" than the conventional crop leading to harm to agriculture, or biodiversity, or both. There are two common concerns:

- The GM crop will be more persistent than the conventional crop in cropped areas, resulting in increased numbers of volunteers appearing the following year causing agronomic problems such as yield loss or increased costs of control.
- The GM crop will be more invasive than the conventional crop in areas outside the crop, resulting in displacement of local plant species and associated fauna, thus having an adverse impact on biodiversity.

Areas outside the crop could be in-field and under management (e.g., field margins), or outside the field and unmanaged (Alix and Coulson 2012; Herman et al. 2013). These definitions are discussed in more detail in "Non-target organisms" and Fig. 2, below. For convenience, the off-crop area is considered as a single entity. In reality, there may be many distinct off-crop areas with varying protection goals.

Another often-mentioned concern is that the transgenes in the GM crop will be transferred to sexually compatible wild plant species. For many crops in many countries this is highly unlikely as sexually compatible relatives of the crop do not occur in the wild (e.g., Raybould and Gray 1993; Stewart et al. 2003). If hybridisation occurs and introgression of the genes is possible, the concern is that conferred new traits will render the wild relatives more persistent in cultivated crop areas, becoming an agronomic problem, or more invasive in areas outside the crop having an adverse impact on biodiversity.

Using the ecosystem services approach, operational protection goals can be defined in order to clarify the concerns and the hypotheses to be tested. In this example, the key ecosystem services to protect would be food production (provisioning service) and biodiversity (supporting and cultural service). There are two distinct spatial areas of protection: in-field and off-field. Whilst in the in-field area the main goal is to protect agricultural production (ensuring that the planting of the GM crop will not compromise the productivity of the crop and subsequent crops). In the off-field area the main goal is to protect native plant species and animals that may rely on them. Considering the different entities of protection and the different spatial contexts the following operational

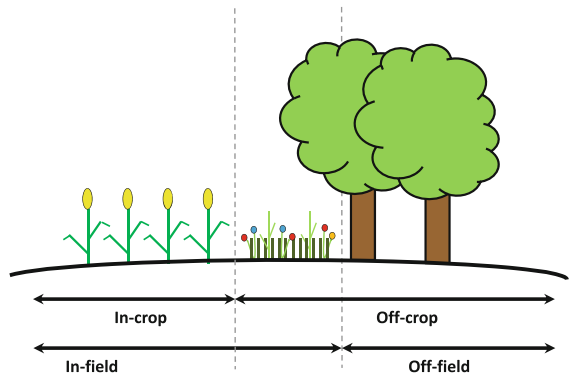

Fig. 2 Off-field/in-field representation

protection goals can be defined. The definition can be expressed in many different ways provided that the entities of protection are made clear, what are they protected from and where (spatial context). Examples are given below:

1. The cultivation of GM crop X in country Y should not result in worse agronomic problems in managed crop areas as a result of increased persistence of the GM crop compared with cultivation of non-GM varieties of this crop.
2. The cultivation of GM crop X in country Y should not result in harm to biodiversity in natural habitats as a result of increased invasiveness of the GM crop compared with cultivation of non-GM varieties of this crop.
3. The cultivation of the GM crop X in country Y should not result in agronomic problems in managed crop areas as a result of increased persistence of wild relatives of the GM crop that have acquired the GM trait.
4. The cultivation of GM crop X in country Y should not result in harm to biodiversity in natural habitats as a result of increased invasiveness of wild relatives of the GM crop that have acquired the GM trait.

The first and third operational goals refer to the protection of agricultural production and the provisioning ecosystem service. The second and fourth goals refer to protection of biodiversity, which may comprise a cultural ecosystem service itself, or provide provisioning, regulating or supporting services.

Once operational protection goals are defined, assessment endpoints can be formulated. These are more specific than the operational protection goals as they include information on the entity to be protected, the attribute and, where possible, spatial and temporal scales and magnitude. Examples of assessment endpoints are given below:

- Establishment of volunteer populations of the GM crop in the managed crop area causing harm to agricultural production in the next crop following the cultivation of the GM plant.
- Establishment of populations of sexually compatible wild relatives that have acquired the GM trait of the GM plant in managed crop areas causing harm to agricultural production in the next crop following the cultivation of the GM plant.

Providing a timescale for protecting displacement of native plant species in natural habitats may prove more difficult as it will depend on the crop under assessment and the ecology of the compatible wild relatives. However, the problem formulation step takes into account this information and helps establishing an appropriate temporal scale.

Defining the assessment endpoints during problem formulation allows risk assessors to predict the probability and extent of adverse effects on those endpoints. This does not necessarily mean that specific tests or studies have to be conducted to predict adverse effects, because there may be enough information on the crop biology and the nature of the trait to provide sufficient evidence to characterise risk.

For most GM crops a comparative assessment of agronomic and phenotypic characteristics is conducted. These studies test the hypothesis that the genetic modification has not changed the phenotype of the donor crop such that cultivation of the GM crop is more likely to lead to adverse effects on the assessment endpoints than is cultivation of the comparator non-GM crop. Measurement endpoints indicative of persistence or invasiveness are included in the study (Table 1). Therefore during problem formulation, a compilation of information on the crop biology, the trait and the comparative assessment may be sufficient to assess the probability of adverse effects on some of the assessment endpoints. If further tests of the hypothesis are needed to increase confidence or reduce uncertainty further data may be acquired.

Non-target organisms

Another area of assessment often considered in ERAs for GM crops is the effect that the use of the GM crop may have on non-target organisms. The definition of non-target organism (NTO) for ERAs of GM crops has been a point of discussion for many years. For GM crops that produce traits aimed at pest control, non-target organisms are considered as all organisms not targeted by the trait. There are many GM crops that do not produce pesticidal traits. Nevertheless, many regulatory frameworks require an assessment of the risk to non-target organisms from their use. The definition of non-target organisms as those not specifically targeted by the trait causes problems for two reasons. First, not all organisms are valued equally; for example, pests not targeted by the crop

Table 1 Example of operational protection goals, assessment endpoints, test hypotheses and measurement endpoints that could be defined for the area of assessment of persistence and invasiveness

Policy protection goals	Operational protection goals	Assessment endpoints	Test hypotheses	Measurement endpoints
Protection of sustainable agricultural production	The cultivation of the GM crop X in country Y should not result in worse agronomic problems in managed crop areas as a result of increased persistence of the GM crop compared with cultivation of non-GM varieties of this crop	Establishment and size of volunteer populations of the GM crop in the managed crop area causing harm to agricultural production in the next crop following the cultivation of the GM plant	The genetic modification has not resulted in potentially harmful changes to the agronomic or phenotypic characteristics of the donor crop that may lead to increased persistence in managed crop areas	Comparison of characters[a] indicative of persistence or invasiveness between the GM plant and a suitable comparator[c] (e.g. seed germination; plant establishment and vigour; time to flowering and maturity; plant height; pollen viability and pollen shed, etc.)
	The cultivation of the GM crop X in country Y should not result in agronomic problems in managed crop areas as a result of increased persistence of wild relatives of the GM plant that have acquired the GM trait	Establishment and size of populations of sexually compatible wild relatives that have acquired the GM trait in managed crop areas causing harm to agricultural production in the next crop following the cultivation of the GM plant	Introgression of the trait into sexually compatible wild relatives[b] has not resulted in potentially harmful changes to characteristics that may increase the invasiveness of the wild relatives in managed crop areas	Comparison of characters[a] indicative of persistence or invasiveness between the GM plant and a suitable comparator[c] (e.g. seed germination; plant establishment and vigour; time to flowering and maturity; plant height; pollen viability and pollen shed, etc.)
Protection of biodiversity	The cultivation of GM crop X in country Y should not result in harm to biodiversity in natural habitats as a result of increased invasiveness of the GM crop compared with cultivation of non-GM varieties of this crop	Displacement of native plant populations and associated fauna due to increased invasiveness of the GM crop in natural habitats compared with the conventional crop	The genetic modification has not resulted in potentially harmful changes to the agronomic or phenotypic characteristics of the donor crop that may lead to increased invasiveness in off-field areas	Comparison of characters[a] indicative of persistence or invasiveness between the GM plant and a suitable comparator[c] (e.g. seed germination; plant establishment and vigour; time to flowering and maturity; plant height; pollen viability and pollen shed, etc.)
	The cultivation of GM crop X in country Y should not result in harm to biodiversity in natural habitats as a result of increased invasiveness of wild relatives of the GM crop that have acquired the GM trait	Displacement of native plant populations and associated fauna due to increased invasiveness of wild relatives of the GM crop that have acquired the GM trait	Introgression of the trait into sexually compatible wild relatives[b] has not resulted in potentially harmful changes to characteristics that may lead to increased persistence or invasiveness in off-field areas	Comparison of characters[a] indicative of persistence or invasiveness between the GM plant and a suitable comparator[c] (e.g. seed germination; plant establishment and vigour; time to flowering and maturity; plant height; pollen viability and pollen shed, etc.)

[a] See Garcia-Alonso (2010) and Raybould et al. (2010) for a list of characters

[b] Where introgression is considered plausible

[c] The suitability of comparator will depend on how decisions will be made. In many studies, the comparator is a non-GM line that is near-isogenic to the GM crop under assessment. In others, several non-GM varieties of the crop may be used as comparators. Use of a near-isoline is a strict test of the hypothesis that no potentially harmful differences were introduced by transformation. Use of several varieties helps to set in context any differences between the GM and non-GM near-isolines

probably have lower value than pollinators. Secondly, not all organisms can be assessed explicitly in the ERA. The objective of protection should therefore be selected carefully (USEPA 2003). The ecosystem services approach can be very useful in clarifying these objectives. We will focus on the assessment of non-target arthropods (NTAs) to keep the example relatively simple.

The policy protection goals that would apply to the ERA of NTAs in most jurisdictions are the protection of biodiversity and protection of agricultural production. When translating these policy protection goals to operational protection goals it is important to remember that agricultural landscapes are heterogeneous: they are a combination of managed crop areas and unmanaged "natural" areas in which different protection goals may apply (Herman et al. 2013).

In the regulatory framework for registration of plant protection products in the EU, there have been many joint activities between regulators, academics and industry to harmonize the approaches for environmental risk assessments of non-target arthropods (NTA). The latest activity was the production of the ESCORT 3 document, which aimed at harmonizing approaches to ERA of pesticides by linking NTA effects testing with protection goals (Alix and Coulson 2012). The ESCORT 3 document provides definitions of the different areas considered in agricultural areas:

- In-crop area: area surface covered by the crop plants including the space between the crop rows.
- In-field area: the in-field area comprises the in-crop area and its boundaries that are *managed by the farmer* in the context of the crop management.
- Off-crop area: area where the product is not intentionally applied.
- Off-field area: area surrounding the in-field area excluding neighbouring in-field areas.

The consensus of the ESCORT 3 working group was that in the in-field area (the area managed by the farmer, including the crop and its immediate surroundings), the main policy protection goal is agricultural production. In this area, the focus is on the ecological functions that support the provisioning service of crop production. In the off-field area, the main policy protection goal is the maintenance of biodiversity to provide cultural, regulating and supporting services. The main interest in biodiversity in managed crop areas is the encouragement of beneficial NTA species and the reduction of harmful species, such as pests. Thus there is an interest in reducing diversity (weeds and pests) while protecting valued functions. The approach to NTA biodiversity protection is therefore different in in-field and off-field areas: while in-field areas the focus may be on "functional biodiversity" (sufficient individuals of the type to maintain functions, regardless of their species), in off-field areas the focus is on "structural biodiversity" (the abundance of particular species) (Moonen and Barberi 2008).

In in-field areas, the main aim is to protect provisioning, regulating and supporting ecosystem services. The main reason for the existence of crops is the production of food, feed and other products for human use; therefore, provisioning is the overarching ecosystem service. Regulating services provided by NTA, such as pollination, pest and disease regulation by biological control and decomposition are important in helping the crop to realise its provisioning role. The NTAs that contribute to a particular service can be very varied; some ecological functions underlying ecosystem services are provided by a range of species, others may be more specialised and may be fulfilled by fewer species. The regulating and supporting services can therefore be protected at different levels: abundance of species that are key contributors to the function, diversity of species that contribute to the same function or the function itself.

In off-field areas, the main aim is to protect populations of NTAs that are charismatic, endangered or protected. These species may rely on regulating and supporting services provided by other species in the off-crop area. Furthermore, organisms that grow and reproduce in off-field areas and forage in in-field areas contributing to the regulating ecosystem service in-field may also be regarded as important.

It is worth noting that in some countries, where large amounts of land are devoted to either urban or agricultural areas with small proportions of wild areas, the protection of charismatic and protected species in in-field areas is also considered an important protection goal. This can be considered in the ERA and included as an assessment endpoint where overlap between protected or endangered species and in-crop or in-field areas can be assessed.

Considering the different entities of protection and the different spatial contexts, operational protection goals can be defined. As discussed in the previous

example, the definitions can be expressed in many different ways provided that the entities of protection are clear. Examples of in-field and off-field operational protection goals are given below:

1. In-field:
   The cultivation of GM crop X in country Y should not result in adverse effects on regulating ecosystem functions provided by NTAs in managed crop areas (in-field) compared with cultivation of non-GM varieties of this crop.
2. Off-field:
   The cultivation of the GM crop X in country Y should not result in adverse effects on NTAs of key conservation value in off-field areas compared with cultivation of non-GM varieties of this crop.

Once operational protection goals are defined, assessment endpoints can be formulated. These are more specific than the operational protection goals as they include information on the entity to be protected (e.g. species, populations or functions), the attribute (abundance, function), the spatial scale (in-field, off-field) and where possible the temporal scale (during the season, the following season, during the time of product approval). These points are illustrated below:

- Adverse effects on regulating ecosystem functions provided by NTAs (pollination, decomposition, predation…) in managed crop areas (in field) during cultivation of the GM crop or in the following season.
- Adverse effects on populations of NTAs that provide regulating ecosystem functions (pollination, decomposition, pest control…) in managed crop (in-field) areas during cultivation of the GM crop or in the following season.
- Population decline of valued NTAs in off-field areas during cultivation of the GM crop or in the following season.

The first assessment endpoint focuses the assessment on ecological functions, whereas the second focuses on populations of NTAs that are known to be major contributors or representatives of regulating functions. The third assessment endpoint focuses the assessment on populations of valued NTAs off-field. The temporal scale to consider will depend on policy objectives. If the objective is for ecological functions to be unchanged at the start of the following growing season, the risk assessment would consider the potential for recovery of NTAs if reduced abundance during cultivation of the GM crop were predicted. If temporary reductions in function were unacceptable, the assessment might consider only the probability of reduced abundance of NTAs during cultivation of the GM crop.

Defining the assessment endpoints during problem formulation allows risk assessors to predict changes that are relevant for characterising risk; that is, potentially harmful changes instead of all possible changes. One of the key steps in predicting potentially harmful changes is identifying hazards. For GM crops that produce proteins intended for pest or disease control, the assessment usually focuses on the characterization of the adverse effects of the pesticidal proteins produced and the levels of exposure of the entities of protection. However, there may be a concern that the genetic modification has unintentionally altered the crop in ways that are harmful to NTAs. For this reason, one of the first steps during problem formulation for all GM crops is to establish whether there are unintended changes in the GM crop that could cause environmental harm.

Assessment of risks posed by unintended changes follows a weight of evidence approach where different sources of information are used as there is no single study that can establish if unintended changes that could be harmful have occurred (Garcia-Alonso 2010). The assessment takes into account information from the molecular characterization conducted on the event and from comparisons of composition and agronomic and phenotypic characteristics.

The molecular characterization provides a first check to assess whether the sequence inserted is as intended or changes have occurred after transformation. It also allows identification of the insertion site and assessment of whether any genes that control important plant functions have been disrupted or if there are any open reading frames that could result in the production of proteins other than the ones intended. However, some molecular changes may not translate into phenotypic changes, therefore comparisons of phenotypic characteristics are usually given more weight in the ERA (Macdonald 2012).

Comparison of composition and agronomic characteristics allow assessment of whether important phenotypic characteristics have been inadvertently modified. If unintended differences are detected, their

potential to cause environmental harm is assessed. If no indications of potentially harmful unintended changes are identified through this process, the assessment can focus on the assessing the hazard and exposure of intended differences between the GM crop and the non-GM counterpart to valued environmental entities or attributes (Garcia-Alonso 2010).

During problem formulation, the risk assessor should use existing relevant information. It is possible that information already available can be used to characterise risk sufficiently to address concerns about the relevant assessment endpoints (Romeis et al. 2009). Specific tests or studies only have to be conducted when problem formulation indicates that they are needed. On many occasions, endpoints measured in one study can be used to address different assessment endpoints. For example, if studies have been conducted on surrogate NTO species to assess the effects of the GM crop on NTOs or functions valued in in-field areas, these data can be used to assess the effects on NTOs off-field, as the species will also be representative for those and exposure levels off-field will be much lower than in-field. As discussed above, in some countries policy protection goals aim at protecting farmland biodiversity, which includes protection of protected or charismatic NTA species in in-field areas. In this case, a relevant assessment endpoint that may be considered, in addition to those listed above, could be: "Population decline of protected or charismatic NTAs in in-field areas during cultivation of the GM crop or in the following season". Information on potential exposure to these organisms can be gathered to establish whether these species will indeed be exposed to the GM crop and, if so, exposure pathways and potential harm can be established to determine whether further data is necessary.

For GM crops that produce proteins for pest or disease control, the ERA focuses on the probability and seriousness of harmful side effects on NTAs from the intended production of those proteins. The general hypothesis under test is that at concentrations produced in the crop during cultivation the proteins have no harmful effects on NTAs. Testing this hypothesis involves comparing the predicted exposure to the protein of various functional groups of NTAs with measurements of the effects of the protein on organism that are representative of those groups (Raybould and Vlachos 2011). There are two important criteria for being representative. First, a representative organism is exposed to the protein through a similar route to the organisms it represents. Secondly, a representative organism has similar or greater sensitivity to the protein than do members of the group that are not tested but are likely to be exposed. In other words, the effects of the protein on a representative species provide conservative predictions about the effects on other species in the group (Raybould 2006).

Conservative predictions about exposure may be made from measurements of protein concentrations in plants grown in the field (see, for example, Raybould and Vlachos 2011). Information about effects of the proteins is usually obtained from laboratory studies using purified protein produced in microbes (Raybould et al. 2013). Data from such studies are applicable to any crop producing the same or similar proteins at concentrations similar to or less than those in the study (Romeis et al. 2009). Therefore, new effects studies may not be needed to complete a risk assessment.

If specific studies are considered necessary, a tiered-testing approach is followed (Garcia-Alonso et al. 2006; Romeis et al. 2006, 2008), carefully selecting relevant NTA species or functions (Romeis et al. 2013), well designed tests (Romeis et al. 2011) and appropriate measurement endpoints (Sanvido et al. 2012). Thus the measurement endpoints will be selected case-by-case, depending on the problem formulation for the GM crop under assessment. Depending on the assessment endpoints selected and the hypothesis tested, measurement endpoints for assessing adverse effects on regulating ecosystem services provided by NTAs in managed crop areas may aim at direct measurements of a particular ecological function (for example measuring the rate of predation of sentinel eggs) or indirect measurements (for example measuring whether exposure to the protein produced by the GM crop leads to lethal effects on an NTA representative of the ecological function). Some examples can be found in Table 2.

Discussion

Policy protection goals are set up in most countries to minimise harm to the environment, humans and animals caused by human activities. Therefore, these protection goals must be taken into account when conducting environmental risk assessments (ERAs) to

Table 2 Examples of protection goals, assessment endpoints, risk hypotheses and measurement endpoints for ERAs of cultivation of a GM crop X producing an insecticidal protein A

Policy protection goals	Operational protection goal	Assessment endpoints	Conservative test hypothesis[a]	Measurement endpoints[a]
Protection of sustainable agricultural production	The cultivation of GM crop X in country Y should not result in adverse effects on regulating ecosystem functions provided by NTAs in managed crop areas (in-field) compared with cultivation of non-GM varieties of this crop.	Adverse effects on regulating ecosystem services provided by NTAs (e.g. pollination, decomposition, pest control) in managed crop areas during cultivation of the GM crop or in the following season.	Exposure to insecticidal protein A produced by GM crop X does not have adverse effect on ecological function N (e.g. predation, pollination) relative to the cultivation of non-GM varieties of the crop.	Direct measurement of the ecosystem function (e.g. rate of predation)[a].
		Adverse effects on populations of NTAs that provide regulating ecosystem functions (e.g. pollination, decomposition, pest control) in managed crop areas during cultivation of the GM crop or in the following season.	Exposure to insecticidal protein A produced by GM crop X does not have a greater adverse effect on the population size of NTA Y (e.g. ladybird) than the cultivation of non-GM varieties of the crop.	Increased mortality of ladybird beetles after exposure to high concentrations of protein A relative to unexposed controls in laboratory studies.
Protection of Biodiversity	The cultivation of GM crop X in country Y should not result in adverse effects on NTAs of key conservation value in off-field areas compared with cultivation of non-GM varieties of this crop.	Population decline of valued NTAs in off-field areas during cultivation of the GM crop or in the following season.	Exposure to insecticidal protein A produced by GM crop X does not have a greater adverse effect on the population size of protected species of NTA P (e.g. monarch butterfly) than the cultivation of non-GM varieties of the crop.	Potential exposure (temporal and spatial overlap and levels of exposure) of NTA P to protein A[b]

[a] Problem formulation is always considered to determine whether specific studies with NTAs will have to be conducted. If this is the case, a tiered testing approach is followed (Garcia-Alonso et al. 2006; Romeis et al. 2006, 2008)

[b] Often laboratory or field studies with protected or endangered species a not permitted. Nevertheless, potential exposure and sensitivity can be predicted to assess potential risk

support regulatory approvals for agricultural biotechnology products. However, policy protection goals set in the legislation are often stated in very broad terms and are too ambiguous to be directly applicable in ERAs. Closing the risk assessment—policy gap requires translation of policy objectives into unambiguous attributes that may be measured or predicted scientifically. In other words, the objectives must be made operational. In the context of environmental risk, policy objectives are the avoidance of harm to the environment, and are called protection goals. Making protection goals operational is, therefore, fundamental to good environmental risk assessment and improving decision-making.

In this paper, we offer proposals on how to make protection goals operational for the environmental risk assessment of GM crops. We begin with very general objectives that are likely to be relevant in most countries: protection of sustainable agricultural production and protection of biodiversity. From these objectives, we derive statements of operational protection goals. These statements have several features in common: they refer to cultivation of a specific GM crop in a given country; they refer to specific habitats within the country—in-field or off-field; and they state that relative to cultivation of non-GM varieties, cultivation of the GM crop should not have adverse effects on ecological functions or organisms

supporting the most relevant ecosystem service(s) in that habitat.

From the operational protection goals, we derive definitions of assessment endpoints. These definitions specify the environmental entities and their attributes that are to be protected, and the spatial and temporal extent of protection. Adverse effects above a certain threshold on assessment endpoints may be taken to indicate harm.

Assessment endpoints are crucial as they are the point at which the risk policy—gap may be closed. They are operational definitions of environmental policy and are the basis for formulating scientific hypotheses to be tested in the risk assessment. At their most general, these hypotheses predict that the intended cultivation of the GM crop will not have adverse effects on the assessment endpoint; that is, it will not reduce the abundance of an NTO, or reduce an ecosystem function, that supports the primary ecosystem service(s) in the relevant habitat. The testing of these hypotheses is the scientific basis of risk assessment.

Testing consists of acquiring data (values of measurement endpoints) that can show whether the hypothesis may be true or false. If the hypothesis is that cultivation of an insect-resistant GM crop will have no adverse effects on biological control, a suitable test is exposure of a representative NTA in the laboratory to concentrations of the insecticidal protein greater than or equal to those predicted in the field. If no adverse effects are observed, the hypothesis is corroborated. Should rigorous tests—conditions under which the hypotheses are most likely to be false—corroborate the hypotheses, one may conclude that cultivation of the GM crop poses negligible environmental risk (Raybould 2006). If adverse effects are observed, the hypothesis may be false, and further testing under more realistic conditions may be undertaken to evaluate it. This is the basis of tiered risk assessment (Garcia-Alonso et al. 2006; Romeis et al. 2008).

The scheme we propose ought to be generally applicable. However, its implementation may vary among countries owing to different priorities and interpretations of environmental and agricultural policy objectives. Our definitions of operational protection goals, assessment endpoints, risk hypotheses and measurement endpoints are illustrative not prescriptive. They illustrate the essential properties of the various stages of making protection goals operational; they cannot define how risk managers and assessors must interpret the policies and regulations under which they work. Finally, our scheme does not offer definitions of the size of an adverse effect that should be considered harmful, nor does it suggest how trade-offs between various ecosystem services ought to be managed. These are essential for decision-making and risk management, but are matters for policy, not risk assessment procedures.

Conclusion

We hope that the methods suggested in this paper will help environmental risk assessors and risk managers to focus on the most significant questions: What is it that we are trying to protect? What effects would we regard as harmful? How may we quickly and confidently characterise environmental risk? How may we make effective decisions in a timely way? For too long, much discussion of environmental risks of GM crops has been conducted in scientific bubble, where scientists argue about the validity of certain studies. Good study design and interpretation are vital (Romeis et al. 2011). However, a study's validity does not guarantee its relevance. A study is only relevant for risk assessment if it tests a hypothesis about environmental harm; and, therefore, operational definitions of protection goals are essential to judge a study's relevance. Without a means to judge the relevance of studies, discussion of the environmental risks of cultivating GM crops will remain volatile because of the huge importance given to small effects in single laboratory studies. Methods to define operational protection goals are the first step towards a more substantial discussion of the environmental risks and opportunities of GM crops.

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