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A semi-quantitative approach to GMO risk-benefit analysis

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Abstract In many countries there are increasing calls for the benefits of genetically modified organisms (GMOs) to be considered as well as the risks, and for a risk-benefit analysis to form an integral part of GMO regulatory frameworks. This trend represents a shift away from the strict emphasis on risks, which is encapsulated in the Precautionary Principle that forms the basis for the Cartagena Protocol on Biosafety, and which is reflected in the national legislation of many countries. The introduction of risk-benefit analysis of GMOs would be facilitated if clear methodologies were available to support the analysis. Up to now, methodologies for risk-benefit analysis that would be applicable to the introduction of GMOs have not been well defined. This paper describes a relatively simple semi-quantitative methodology that could be easily applied as a decision support tool, giving particular consideration to the needs of regulators in developing countries where there are limited resources and experience. The application of the methodology is demonstrated using the release of an insect resistant maize variety in South Africa as a case study. The applicability of the method in the South African regulatory system is also discussed, as an example of what might be involved in introducing changes into an existing regulatory process.

Keywords Genetically modified organisms · Risk assessment · Risk-benefit · Regulation

Abbreviations

GMO	Genetically modified organism.
CPB	Cartagena protocol on biosafety
UNCED	United Nations conference on environment and development
PP	Precautionary principle
Bt	*Bacillus thuringiensis*
EFSA	European food science authority
RIAM	Rapid impact assessment matrix
EIA	Environmental impact assessment
SEA	Strategic environmental assessment
RBS	Risk-benefit score
AS	Agriculture score
FS	Food score
ES	Environment score
HS	Health score
SS	Socio-economic score
P	Probability or likelihood
NEMBA	National environmental management biodiversity act

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Introduction

With the introduction of any new technology comes much soul searching and consideration of the potential impacts on health, the environment and society. This applies particularly to genetically modified organisms (GMOs) and more recently to other emerging fields such as nanotechnology and synthetic biology. The concepts in this paper, while focusing on GMOs, may equally well be applied to other new technologies.

World-wide, legislation with respect to GMOs has tended to focus on the risks of the technology rather than the benefits. The governments of countries that have been at the forefront of the adoption of the technology, such as Argentina, have inherently recognized the benefits although they may not have explicitly captured this aspect in their legislation (Laursen 2010). In contrast, countries that have been slow to approve commercial plantings of GM crops, such as Australia, have tended to focus on risks rather than benefits (Linacre et al. 2006a).

The focus on risks has particularly influenced the European attitude to the release of GM crops. Drobnik (2008) points out that all EU directives related to GMOs refer only to assessment of risk, without consideration of benefits.

However, even in Europe there is a groundswell of change in attitude. An improved Risk Analysis Framework was developed as part of the SAFE FOODS project (funded under the EU 6th Framework Programme) and its applicability to GMOs was evaluated (Kuiper and Davies 2010). This framework proposes the assessment of benefits as part of the risk assessment. The authors recommend that the current EU regulatory framework for GMOs should be revisited to incorporate their proposals.

Even without changes in the current EU regulatory framework, Winter (2008) argues that, at least in terms of environmental risk, there is some leeway concerning the legal definition of adverse effect, and that some other criterion than harm avoidance is needed in order to determine what residual risk shall be tolerated or not. Such a criterion could in fact be the environmental benefit arising from the release of the GMO, which could result in an overall decision of no adverse effect.

In view of the increasing calls for consideration of the benefits of the products of GM technology as well as the risks, the time is now ripe for the development of a simple methodology that may be used to facilitate a risk-benefit analysis and serve as a decision support tool for regulators.

The need for a structured approach to risk-benefit analysis

Despite increasing discussion of the need for analysis of the benefits of GMOs as well as the risks, the methodologies by which this might be done are not well defined.

From a regulatory perspective, risk assessors and risk managers have a duty to undertake a risk analysis or risk-benefit analysis in a responsible and transparent manner. When any decision is reached by a regulatory agency regarding an activity involving GMOs, it is common practice to publish a narrative summary that explains the issues that were considered and the reasoning that led to the final decision. It is rare that any quantitative or semi-quantitative analysis is undertaken. An argument against a quantitative approach has been that there are too many unknowns. However our knowledge of, and confidence in, GM technology has increased over the years. GMOs have been in commercial use for over 14 years (James 2009) and a wealth of experience has been accumulated, thereby helping to reduce the level of uncertainty.

In reality, decisions to release a GMO are made despite some uncertainties. Regulators will intuitively use their own backgrounds and perspectives to analyse the data. Decisions based on a (semi)-quantitative approach to risk assessment should also be grounded in clearly defined decision-making criteria. Depending on circumstances, considerations of risk (and sometimes benefit) may encompass food, nutrition, health, environment and socio-economic issues.

It is apparent that there is a need for new tools that will assist the risk assessor and risk manager to undertake at least a semi-quantitative risk-benefit analysis, in order to facilitate balanced consideration of all the complex issues and to take account of uncertainties. At the same time it should be made clear that the inclusion of benefits is not intended to mask risks. Any new tool would not replace the qualitative consideration of the issues at stake, but

could provide additional confidence in the process and facilitate decision-making.

Public perception and risk-benefit acceptance

A logical approach to risk-benefit analysis would demand that there should be a balanced trade-off between benefits and risks. Unfortunately perceptions of risk and benefit are frequently at odds with such a logical approach. The seminal paper by Slovic (1987) outlines the "psychometric paradigm" which emphasizes the fact that people's quantitative judgment of the acceptability of risk is also influenced by additional considerations such as feelings of dread, lack of control, catastrophic potential, and fear of the unknown. As pointed out by Amin et al. (2007), there is a wide gap between how scientists and risk experts think about, define and evaluate risks compared with the lay public. Slovic also demonstrates that the acceptability of risk-benefit trade-offs varies between cultures, societies and groups. Some of these issues were highlighted in the case study on GMO acceptance in China by Swart et al. (2007–2008).

In the case of GMOs, the beneficiaries of the technology are frequently different from those who carry (or who perceive themselves to carry) the risk. It has often been pointed out that one factor inhibiting the acceptance of first generation GM crops (mainly with pest resistance and/or herbicide tolerance) is the fact that commercial farmers, seed producers and agrochemical companies are generally seen to reap the benefits, while the consumer takes the risk in terms of consumption of potentially "unsafe" food. Second generation GM crops will need to show clearer consumer benefits (in terms of cost, quality, nutritional content, availability etc.) if they are to achieve a broader level of acceptance (Qaim 2009; Giannakas and Yiannaka 2008).

The fact that additional considerations influence the ultimate perception of risk, results in an inherently unlevel playing field where people's judgments tend to be biased towards consideration of risk rather than consideration of benefit. This trend is encapsulated in the Precautionary Principle (PP) which forms the basis for the internationally binding Cartagena Protocol on Biosafety (CPB) (Secretariat of the Convention on Biological Diversity 2000). As framed in Principle 15 of the Rio Declaration (United Nations Conference on Environment and Development (UNCED) 1992), the PP states:

> Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation

Other definitions of the PP (Wingspread 1998) take into account human health as well as the environment. The PP has been criticized by many, as summarized by Vlek (2010), who points to its inherent pessimism regarding uncertain risks. Vlek proposes an alternative "venture principle" where instead of the feared "serious harm" calling for precaution, an equally uncertain opportunity for benefit might tempt the proponent to take positive action: "nothing ventured, nothing gained". The fact that this alternative venture principle is generally not considered in international or national legislation no doubt contributes to the skewed bias towards risk rather than benefit.

In the event that it is possible to carry out a quantitative, or at least semi-quantitative, risk-benefit analysis of GMOs, it would be valuable to be able to define a perceived acceptable risk-benefit ratio that can be used to reach decisions (to approve or not to approve an activity involving GMOs) as a result of such an analysis. This risk-benefit factor may not be the same for all societies or situations. The early paper of Starr (1969) concluded that the acceptability of risk from an activity is roughly proportional to the third power of the benefits for that activity, at least in instances where technology adoption is involuntary (as can be assumed for the case of GMOs). Subsequent publications have challenged Starr's analysis, and more recent publications point to a wide range of additional factors that influence acceptance, such as whether the benefits accrue to single individuals or to society as a whole (Costa-Font et al. 2009).

Although this paper outlines a methodology to analyse the balance of risk vs benefit in a non-biased manner, the decision-making process that normally occurs at national level would logically take into account societal factors and the need to ensure that decisions made will achieve sufficiently broad public acceptance.

Risk-benefit analysis methodologies for GMOs

To date, ex ante GMO analyses that explicitly cover benefits as well as risks are few and far between. The majority are descriptive and qualitative. Moreover they are usually one dimensional (e.g. looking at food risks vs food benefits, or environmental risks vs environmental benefits). Kostandini et al. (2009) have undertaken an ex ante analysis of the benefits of transgenic cereal crops in low-income countries, but did not at the same time examine the risks. Dawe and Unnevehr (2007) examined the benefits to consumers of GMO Golden Rice, taking into account the hurdles that still need to be overcome to demonstrate its safety and appropriateness. Espinoza-Esquivel and Arrieta-Espinoza (2007) described an environmental risk-benefit analysis for the deployment of GM rice in Costa Rica.

In any risk-benefit analysis, the alternative scenarios (either no action or an alternative action) should also be considered and compared. Unfortunately this is generally not the case, and can lead to decision making that is either not contextualized or that assumes the decision to introduce or not to introduce a GMO is the only decision to be made. This issue is becoming even more important with the emergence of a range of new biotechnologies that may bypass current process-based legislation (Morris and Spillane 2008).

Although rarely implemented, several papers have made reference to the possibility of using computer based risk assessment tools such as Monte Carlo simulation approaches and Bayesian statistical analysis to assist in risk analysis of GMOs, particularly to define possible outcomes in the light of uncertainties in the analysis (e.g. Hill and Sendashonga 2003; Linacre et al. 2006b). Unfortunately this requires the risk assessor and the risk manager to have a good understanding of statistical methods and the use of relevant computer programmes. Where there is a lack of understanding of the methodology, there is a danger that the user may regard any programme as a "black box" and accept the output without understanding the processes involved. In addition, many relevant computer programs are proprietary and relatively expensive, therefore not easily accessible by regulators in the developing world where there is a particular need for assistance with risk analysis methodologies.

It is therefore appropriate to examine the potential for simpler methodologies that could be relatively easily applied to the classical methodology for GMO risk assessment, with appropriate modification to risk-benefit assessment, namely the steps of:

(1) Hazard or positive effect identification and characterization[1]
(2) Assessment of likelihood of the hazard or positive effect materializing
(3) Assessment of the magnitude of the effect in the event of the hazard or positive effect materializing
(4) Overall characterization of the risks or benefits in terms of the combined likelihood and magnitude

The RIAM methodology

One possible tool that could be modified and adapted towards a semi-quantitative GMO risk-benefit assessment is the Rapid Impact Assessment Matrix (RIAM), which was developed originally as a tool for Environmental Impact Assessment (EIA) (Pastakia and Jensen 1998).

The RIAM methodology was not designed with GMOs in mind and suffers from some limitations in its applicability for this purpose. Nevertheless it has been applied to EIA of GM rice (Bermúdez Muñoz and Víquez Camacho 2010). The applicability of RIAM to Strategic Environmental Assessment (SEA) has also been tested (Kuitunen et al. 2008). SEA has been proposed as a useful method at the stage of

[1] In this paper, the following definitions have been applied:
Hazard The potential of an organism to cause harm
Harm The magnitude of the consequences of a negative effect, if it should occur
Risk The combination of the magnitude of the consequences of a hazard, if it occurs (i.e. harm), and the likelihood that the consequences will occur
Positive effect The potential of an organism to cause beneficial effects or reduce adverse effects, i.e. the opposite of hazard
Potential benefit The magnitude of the consequences of a positive effect, if it should occur, i.e. the opposite of harm
Benefit The combination of the magnitude of the consequences of a positive effect, if it occurs (i.e. potential benefit), and the likelihood that the consequences will occur, i.e. the opposite of risk.

planning of GMO projects, where alternative biotechnology options can be considered (Linacre et al. 2006b).

The RIAM as originally developed and applied up to now, focuses on environmental issues and addresses the third step in risk assessment, namely the assessment of the magnitude of the effect. It provides a method of scoring within a matrix that has been designed to allow subjective judgements to be quantitatively recorded.

The standard RIAM methodology would normally be used following a scoping exercise to identify and characterize the components that would constitute the hazards or positive effects (step 1 above; step 2 does not form part of RIAM—see below).

These would then be assessed (step 3) in terms of various criteria as follows:

(A) Criteria that are of importance and can individually change the overall assessment
(B) Criteria that are of value, but not of sufficient importance to be individually capable of changing the final assessment

The identified hazards or positive effects are categorized in terms of their importance under Group A, or in terms of their permanence under Group B.

The basic formula for the RIAM is (Pastakia and Jensen 1998):

$$A1 * A2 = (AT)$$

$$B1 + B2 + B3 = (BT)$$

$$(AT) * (BT) = ES$$

The final score is designated in this paper as RBS (Risk-Benefit Score) as an alternative to ES (Environmental Score), the term used by Pastakia and Jensen. A1 is the importance of impact, measured on a scale of 0–4 (no impact to major impact), A2 is the magnitude of the change/effect measured on a scale of -3 to $+3$ (major negative change to major positive change), B1 is the permanence of the impact-causing activity measured on a scale of 1–3 (no change/not applicable to intended permanent change), B2 is the reversibility of the impact measured on a scale of 1–3 (not applicable to irreversible) and B3 is the accumulation of impact measured on a scale of 1–3 (no change/not applicable to cumulative or synergistic impact). Ijas et al. (2010) suggested the addition of an additional criterion B4, which would represent the susceptibility of the target environment. However they also pointed out that the A1 and A2 criteria have the major effect on the overall results. For the purposes of a GMO risk assessment, it would be appropriate to include the criterion of susceptibility of the receiving environment or population, but the criterion of permanence of impact could justifiably be excluded, since it is inherently included in B2 (reversibility). Moreover no crop is planted in perpetuity, in comparison with (say) a dam, which is intended to be permanent.

The RIAM method requires the assessor to assign A and B scores for each component under consideration. For each component a score is generated which is then assigned to a "range band". The numbers of values within each range band are then added to give an overall view of the positive and negative scores for a certain set of considerations (e.g. environment, socio-economic) or across all considerations. As framed in the RIAM method, the main use would be in comparison of options for action (e.g. use of a GMO rather than use of an alternative technology, or the effect of various risk management options).

While the use of the RBS (with or without the use of range bands) is useful in comparing like with like (e.g. environmental positives vs environmental negatives) or in obtaining a comparison between options, in its original form it is not applicable for the comparison of e.g. environmental risks/benefits vs health risks/benefits. This is because it does not make any adjustment or correction for the number of different parameters that might be evaluated in each case. If more components are analysed for the environment than for health, the overall weighting will automatically be swayed towards the environmental considerations.

The exclusion of probabilities or uncertainties (step 2 of the risk assessment) from the RIAM methodology is fairly common in ecological impact assessment (Tennøy et al. 2006). The exclusion of probabilities appears particularly inappropriate when benefits are balanced against risks, since the likelihood of a hazard materializing may be of a very different order of magnitude from the likelihood of a positive effect being realized.

It is therefore clear that for the purposes of a GMO risk-benefit assessment, an additional term needs to be included that addresses the second step, namely the likelihood of the hazard or positive effect

materializing. Moreover the results need to be interpreted in a way that would allow categories of risks and benefits to be compared in a multi-dimensional framework. Although it may not be appropriate to give equal weighting to issues of (e.g.) environment, agriculture, food and health, the decision to afford bias to any of these areas should be a function of the regulators concerned, not of the process that was used to undertake the assessment.

A modified methodology for GMO risk-benefit assessment

A modified methodology is proposed below that takes the factors cited above into account. Taking environmental considerations as an example, for each component under consideration (i.e. hazards or positive effects that have been identified and characterized in step 1 of the risk assessment), we assign values as before:

$$A1_1 * A2_1 = AT_1$$

$$B1_1 + B2_1 + B3_1 = BT_1$$

where subscript 1 denotes component 1.

The definitions remain the same as in the original RIAM methodology, except for B1 which is redefined to represent the susceptibility of the receiving environment and/or affected population.

To reach an Environment Score (ES_1) for that component we then multiply the A and B totals as before, but include a factor P that provides an estimate of the likelihood of the hazard or positive effect materializing:

$$AT_1 * BT_1 * P_1 = ES_1$$

The overall score for ES will then be computed as the sum of the individual scores divided by the number of components evaluated and determined to have a non-zero score (n).

$$(ES_1 + ES_2 \ldots ES_n)/n = ES$$

Similarly scores can be calculated for Agriculture (AS), Health (HS), Food (FS), Socio-economic factors (SS) or any other issue that is deemed to be relevant.Finally, to achieve an overall RBS:

$$RBS = aES + bAS + cHS + dFS + eSS$$

The factors a, b, c, d and e represent optional weightings that may be assigned to each category, and may be modified based on the specific situation provided that the same relative weightings are used in any comparison of options (e.g. alternative risk management measures). Any weightings of this nature should be agreed before the risk-benefit analysis is undertaken, to avoid later manipulation to achieve some desired result.

In consideration of the fact that the final output is now a Risk-Benefit Score covering a range of issues, and not just an Environmental Score, the assessment criteria are applied according to Table 1.

The nature of this methodology tends towards a product based rather than a process based assessment (i.e. focusing on the characteristics of the GMO itself rather than the process that was used to create it). Nevertheless, a detailed understanding of the GMO at the molecular level will still be required, particularly to identify possible unexpected effects that might result at the phenotypic level, and will contribute towards the assessment.

Identification of hazards and positive effects leading to harm or potential benefit

In order to facilitate the initial scoping step of the risk-benefit analysis, it is appropriate to identify some common considerations or issues that may arise, depending on the particular GMO under evaluation. The focus here is on GMOs intended for release rather than contained use. The majority of GMOs currently evaluated by regulatory authorities around the world are crops engineered for herbicide tolerance (the most common being glyphosate tolerance) or pesticide resistance (generally using a variety of genes coding for proteins from the soil microorganism *Bacillus thuringiensis* (Bt)). Other crop traits under development include drought tolerance (and tolerance to other abiotic stresses), resistance to a variety of biotic stresses (bacterial, fungal, viral), crops with enhanced nutritive value, and crops engineered to produce a variety of pharmaceuticals and chemicals.

Beyond GM crops, other GMOs that may be considered for release by regulatory authorities include GM fish or other animals, insects, recombinant vaccines, and microorganisms. However given that the major focus is currently on crop plants, the issues highlighted below are primarily concerned with crops. They may be used to provide some guidance in the

Table 1 Definition of criteria for assigning scores

Criterion	Scale	Description
A1. Importance of the impact	4	Important to the population or the environment as a whole, goes beyond national interests
	3	Important at national level to the population or the environment
	2	Important to areas or to population groups immediately outside the local condition
	1	Important to a small group of people or to a small location
	0	No importance or not relevant
A2. Magnitude of change	+3	Major positive effect
	+2	Significant improvement in status quo
	+1	Improvement in status quo
	0	No change to status quo
	−1	Negative change to status quo
	−2	Significant negative disadvantage or change
	−3	Major negative disadvantage or change
B1. Susceptibility of the environment or affected population	3	Extremely sensitive environment or population
	2	Some sensitivity in the environment or population
	1	No change/not applicable
B2. Reversibility of impact	3	Impact will change the environment or affected population irreversibly or restoration will last at least 10 years
	2	Reversible impact; the GMO can be easily withdrawn and the situation restored to the status quo
	1	No change/not applicable
B3. Cumulativeness/synergism of impact	3	The activity will have obvious cumulative or synergistic effects with other activities (e.g. other GMO events) in the same area
	2	May be some cumulative or synergistic effects but their effect is likely to be relatively small
	1	No cumulativeness/Not applicable
P. Probability or likelihood of occurrence[a]	1	Certain
	0.93	Almost certain
	0.75	Probable
	0.5	Chances about even
	0.3	Probably not
	0.07	Almost certainly not
	0	Impossible

[a] Descriptors taken from article on "Words of estimated probability" in Wikipedia http://en.wikipedia.org/wiki/Words_of_Estimative_Probability#cite_note-CIAKent56-1

identification and characterization of hazards and positive effects, but are by no means exhaustive. Any decision to include a particular hazard or positive effect as part of the risk-benefit analysis should be made only in the context that it is necessary to make a sound judgement. Superfluous data may be confusing to the regulators and add to the time and costs required to reach a decision (Craig et al. 2008).

The various issues are categorized under the headings of Environment, Agriculture/Agronomy, Food/feed and Nutrition, Health and Socio-economic considerations, with some discussion under each section. For each issue some hazards and/or positive effects are identified as relevant.

Environmental considerations

Much has been written concerning the ecological effects of GM crops (e.g. Conner et al. 2003; Warwick et al. 2009) and it is impossible to do more

Table 2 Some possible environmental considerations for a GMO release

Consideration	Hazard leading to harm	Positive effect leading to potential benefit
Land use	Development of crops suited to extreme environments encourages conversion of pristine land to agriculture	Increased productivity lessens need to bring new land into production
Soil erosion	More intensive agriculture increases soil erosion	Low-till or no-till agriculture reduces soil erosion and run-off
Greenhouse gas emissions	More intensive agriculture and new land use increases greenhouse gas emissions	Shift to low-till or no-till agriculture reduces use of fossil fuels and greenhouse gas emissions
Water use and quality	Increased water use due to new land in production and more irrigated crops	Drought tolerance reduces need for irrigation
		Reduction in use of harmful agrochemicals with long half life results in less residues in water supplies
Herbicide usage	Increased use of herbicides on herbicide tolerant crops	Herbicide tolerant crops permit shift from toxic to environmentally benign herbicides
	Emergence of herbicide tolerant weeds	
Pesticide usage	Need to introduce new sprays for secondary pests	Reduction in use of pesticide sprays on pest resistant crops
	Emergence of resistant pests	
Usage of other agrochemicals (fertilizers etc.)	Increased usage linked to more intensive agriculture	Reduction in use or shift to less harmful chemicals
Invasiveness of GMO	Increased weedy characteristics compared with conventional counterpart as a result of increased environmental fitness	Decreased weediness compared with conventional counterpart due to reduced environmental fitness
Non-target organisms	Emergence of new agricultural pests due to reduced use of broad-spectrum sprays	Unintended effects on birds, mammals, micro-organisms etc. positively influence biodiversity (either directly or indirectly through changes in agricultural practices)
	Unintended effects on birds, mammals, micro-organisms etc. negatively influence biodiversity (either directly or indirectly through changes in agricultural practices)	Reduced use of broad spectrum sprays enhances biodiversity
Gene flow to wild crop relatives	Gene flow results in increased fitness of weedy relatives, or extinction of threatened populations due to decreased fitness	Gene flow results in decreased fitness of weedy relatives
	"Contamination" of biodiversity by introduced genes[a]	
Biological diversity	Loss of biodiversity	Improvement in biodiversity through altered agricultural practices

[a] This should be contextualized to take into account the fact of pre-existing gene flow between conventional crops and their wild relatives. Transfer of introduced genes may not cause any additional significant impact

than summarize some of the issues in Table 2. Environmental considerations for a GMO release are of a somewhat different nature from those generally considered in an environmental impact assessment. While some data may be obtained in field trials, or lessons may be learned from releases that have taken place elsewhere in the world, the argument has been made that it is impossible to be able to predict in advance changes that may take decades or centuries to materialize. Such future changes, if they occur, may be either harmful or beneficial, but care must be taken in any ex ante assessment not to put too much weight to purely hypothetical considerations.

Agricultural/agronomic considerations

To a great extent, the agricultural or agronomic considerations that will determine adoption of technology by farmers relate to economic risks and benefits. However farmer profitability as a direct measure should rather be assessed separately under socio-economic considerations (see below). Issues

Table 3 Some possible agricultural and agronomic considerations for a GMO release

Consideration	Hazard leading to harm	Positive effect leading to potential benefit
Yield and other agronomic characteristics	Metabolic burden of introduced genes results in decreased yield	Enhanced performance of GM varieties leads to increased yield
Abiotic stress tolerance	Expected performance not realized when abiotic stress is unpredictable (e.g. drought)	Stress tolerance results in ability to grow crops on marginal land, assist in adaptation to climate change
Bacterial/fungal/viral disease resistance	Disease resistance may break down. New diseases may emerge to fill the ecological niche	Increased resistance to disease leads to higher yields
	Possible negative effects on growth promoting symbionts	
Development of pest resistance to Bt toxins	Pest resistance results in Bt being rendered ineffective due to pests becoming resistant	
Organic farming and/or conventional agriculture	Cross-pollination from nearby GM crops results in value loss for non-GM crops	Trend to accept GMOs as part of organic farming (Ronald and Adamchak 2008) could assist organic farmers to meet their objectives
Monoculture	Reduction in genetic variability leading to increased susceptibility to new diseases	

listed in Table 3, while having an indirect impact on profitability, should be considered in their own right.

Food/feed and nutrition considerations

In 2006 the European Food Science Authority (EFSA) held a colloquium to debate methods and approaches to risk-benefit analysis of foods. This colloquium considered foods in general, with no specific mention of GMOs. Moreover it considered a range of issues and measures that are unlikely to be able to be addressed in an ex ante food safety assessment such as would be carried out prior to regulatory approval of a GMO or GM food or feed, such as disability adjusted life years (DALYs). More recently EFSA (EFSA Scientific Committee 2010) has produced a guidance document on human health risk-benefit assessment of foods, which starts to define composite metrics for risk-benefit assessment, though once again these would not be entirely appropriate for ex ante risk analysis of GMOs.

The balance between positive and negative effects will generally depend on intake patterns of a particular food, leading to the concept of a "window of benefit" as described by Palou et al. (2009). The exposure to a food should be taken into account in the risk-benefit assessment.

The issues listed in Table 4 are those frequently considered in any GMO risk assessment, and while it may not be possible to assign values to them with the degree of rigour demanded by EFSA for conventional foods that are already widely consumed, nevertheless at a semi-quantitative level it is should be possible to make an informed judgement.

Health considerations

Much of the literature concerning the health effects of GMOs relates to issues of food safety and nutrition. Depending on the particular GMO under review, the review team could optionally decide to condense the health and food issues into a single risk-benefit score.

However there are a number of other health-related considerations that apply to certain GMOs, some of which are itemized in Table 5. A particular secondary health benefit that has been noted in some GM crops is the reduction in illness amongst farm workers as a result of occupational exposure to pesticides (Huang et al. 2006).

Socio-economic considerations

Falck-Zepeda (2009) discusses in some detail the issues concerning the inclusion of socio-economic considerations in the risk analysis process. The

Table 4 Some possible food/feed and nutrition considerations for a GMO release

Consideration	Hazard leading to harm	Positive effect leading to potential benefit
Allergenicity	Increased allergenicity leads to adverse effects	Decreased allergenicity results in less adverse reactions
Toxicity	Increased toxicity (acute or chronic) results in more adverse effects	Decreased toxicity (acute or chronic) results in fewer adverse effects
Food with altered nutritional value	Altered intake of certain nutrients leading to adverse effects	Overcoming nutritional deficiencies
Microbial safety	Increased danger from known or novel pathogens	Increased shelf life, decreased contamination from bacterial or fungal pathogens
Food processing	Unexpected negative effects arise when food is processed	Enhanced processing (e.g. from introduction of processing enzymes)

Table 5 Some possible health considerations for a GMO release

Consideration	Hazard leading to harm	Positive effect leading to potential benefit
Antibiotic resistance	Transfer of antibiotic resistance markers to pathogenic microbes results in reduced antibiotic efficacy	
Plant made pharmaceuticals	Accidental admixture with conventional crops, resulting in inadvertent exposure to pharmaceuticals	Lower cost of production, absence of human pathogens
Health effects arising from exposure of farm workers to toxic agrochemicals		Reduction in spraying of toxic pesticides and herbicides
Live GM vaccines	Ability to colonize host and result in carrier status	More effective vaccine
	Gene transfer to other organisms. Reversion of an attenuated strain	

regulatory requirements (or their absence) for socio-economic analysis vary considerably between countries. Moreover in some systems socio-economic considerations are integrated with consideration of other aspects of biosafety, whereas in others they would be separately evaluated. Whichever approach is adopted, the socio-economic analysis will contribute to the final decision making. Falck-Zepeda argues persuasively that socio-economic analysis should be undertaken only in the final regulatory stage of commercialization or propagation, but not at the laboratory or field trial stages. He also stresses that the issues considered in a socio-economic analysis that will be used for regulatory decision making should realistically be limited to those that can be estimated meaningfully in an ex-ante study.

From an economic perspective, a useful review of the economic impact of GM crops world-wide is provided by Gómez-Barbero and Rodríguez-Cerezo (2006).

Socio-economic considerations are summarized in Table 6.

The risk-benefit analysis in practice

The new tool for risk-benefit analysis of a GMO was tested in practice, using as an example Syngenta's Bt11 maize assessed for release in South Africa. This was selected in part because the event was intensively scrutinized during an appeal that was lodged against the approval for conditional general release (Morris et al. 2005). Bt11 maize contains a variant Cry1Ab protein from *Bacillus thuringiensis,* which confers resistance to lepidopteran insect pests. It also contains a gene coding for phosphinothricin-N-acetyltransferase (PAT) from *Streptomyces viridochromogenes*, conferring tolerance to the herbicide glufosinate ammonium. However glufosinate is not registered for use on the crop.

The most important issues considered in the South African decision to approve conditional general release of this event were used as a basis for the scores given in Table 7, supplemented by the EFSA scientific opinion on Bt11 (EFSA 2005) and the information provided by the International Life Sciences Institute

Table 6 Some possible socio-economic considerations for a GMO release

Consideration	Hazard leading to harm	Positive effect leading to potential benefit
Control over tools and relation to production	Increased control by multinational seed companies reduces consumer choice	Multinational companies able to ensure reliable supply of high quality seed
Farmer profitability	High seed cost leads to reduction in income potential	Better performing seeds result in increased income and profitability
Trade	Bias against GMOs has negative impact on exports and/or competitiveness[a]	Increased production leads to higher export potential
Rural labour	Less need for labour, and/or consolidation of farm ownership results in increased rural unemployment	Increased profitability leads to increased rural employment and/or alternative options for employment
Cultural traditions, knowledge and practices	Loss of traditional crops or food plants, farmers' varieties and indigenous technologies	
Food security	Unexpected effects result in crop losses, and/or shift to production of non-food crops	Increased food production leading to increased food security. Crops less susceptible to extreme climatic conditions
Religious and ethical considerations	Increased cost to segregate GM products to address religious and ethical concerns	
Food aid	Food aid not provided to populations in need, due to unwillingness/inability of governments to accept GM food	Increased availability of food for distribution to populations in need
	Increased cost and food safety hazard due to requirement to mill grain before distribution	

[a] Loss of competitiveness may result from a decision *not* to introduce a GMO, highlighting the need for comparison of options

(ILSI) Centre for Environmental Risk Assessment online crop database.[2] Assignment of scores was initially undertaken by the author, and subsequently cross-checked with other individuals with considerable experience of risk assessments in the South African regulatory system.

At the time of the original analysis, provision for inclusion of socio-economic considerations had not been incorporated into the GMO Act. The scoring for socio-economic issues (SS) below is therefore used to provide an example of how this might be done rather than as a reflection of the actual assessment carried out for Bt11. The impact on rural employment is likely to be greatest for herbicide tolerant maize that lends itself to no-till agriculture. Although Bt11 contains the gene coding for glufosinate tolerance, this herbicide was not registered for use on the crop and therefore the assumption is that herbicide usage on the crop will not change. The SS score should be treated with circumspection because there are a number of uncertainties as to the actual socio-economic impact.

In the current paper it is not possible to provide detailed justification for the assigned scores. In addition the fact that the scores represent the views of only a small number of people means that they have not been fully validated, and should therefore be regarded as only illustrative of the methodology.

The results are presented graphically in Fig. 1.

It is apparent that in this instance the overall RBS is positive (possible range of RBS values is −540 to +540), justifying the decision of the South African regulatory authorities to approve the release. Only in instances where there is need to balance an overall risk of one type against an overall benefit of another type (e.g. ES vs SS) would the decision be more controversial.

The methodology was also tested for a few more controversial GMOs that have not been released or have been released only in a few jurisdictions. In these cases less information was available about the GMO; it was necessary to make some assumptions

[2] Bt11 information available from http://www.cera-gmc.org/?action=gm_crop_database&.

Table 7 Risk-benefit assessment of Bt11 maize

Issues considered	A1	A2	B1	B2	B3	P	Score
ES							ES_{1-4}
Risks							
Negative effects on non-target organisms	3	−1[a]	1	2	2	0.3	−4.5
Outcrossing to wild relatives of maize	0	0	1	1	2	0	0
Unapproved use of glufosinate on maize	1	0	1	2	2	0.5	0
Benefits							
Decreased pesticide use	2	2	2	2	3	0.75	28.0
							ES = +11.75
AS							AS_{1-3}
Risks							
Development of pest resistance to Bt	3	−3	2	3	3	0.07[b]	−5.0
Outcrossing to conventional maize	1	0[c]	1	1	1	0.93	0
Benefits							
Increased yield	3	2	1	1	1	0.75	13.5
							AS = +4.3
FS							FS_{1-4}
Risks							
Introduced proteins cause allergic response	1	−2	2	2	1	0.07	−0.7
Introduced proteins are toxic	3	−3	3	3	1	0	0
Unintended negative compositional changes	3	−1	2	2	1	0.07	−1.05
Benefits							
Decreased mycotoxin contamination	3	+2	1	1	1	0.5	9.0
							FS = +2.4
HS							HS_1
Risks							
None foreseen							
Benefits							
Decreased occupational exposure to pesticides	1	+2	2	1	1	0.75	6.0
							HS = +6.0
SS							SS_{1-6}
Risks							
Increased control by multi-national seed companies	1	0	1	1	1	0.75	0

Table 7 continued

Issues considered	A1	A2	B1	B2	B3	P	Score
Negative impact on exports	3	−1	2	1	1	0.3	−3.6
Negative impact on rural employment[d]	2	0	2	2	3	0.3	0
Negative impact on organic production (cost of segregation)	2	−1	2	2	1	0.5	−5.0
Benefits							
Increased farmer profitability	2	2	1	1	2	0.93	14.9
Rural women and children in small-scale farming freed from manual labour	1	1	1	1	2	0.75	3.0
							SS = +2.3
					Overall RBS		26.75

[a] This value may become positive (i.e. a risk may become a benefit) if comparison is made with conventional pesticides that cause more damage to non-target organisms

[b] The probability of insect resistance to Bt occurring can be minimized by appropriate risk management measures

[c] The assessment of no change to status quo was based on the effect on agricultural production. Organic farmers may have a different assessment

[d] The impact on rural employment is likely to be greatest for herbicide tolerant maize that lends itself to no-till agriculture. Although Bt11 contains the gene coding for glufosinate tolerance, this herbicide was not registered for use on the crop and therefore the assumption is that herbicide usage on the crop will not change

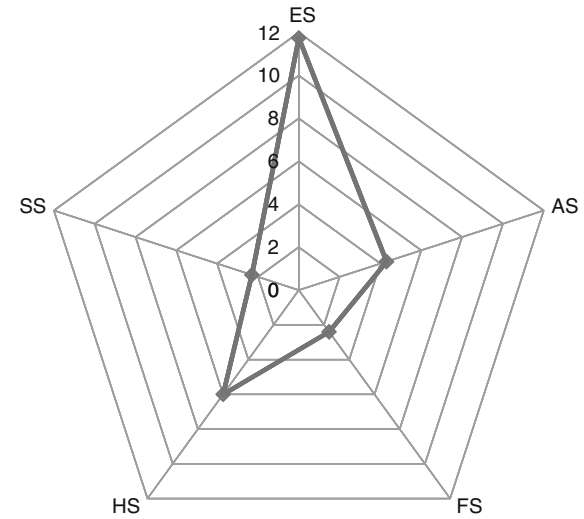

Fig. 1 Graphical representation of the results of risk-benefit assessment of Bt11 maize

and the results summarized in Table 8 are therefore merely indicative of the scores that might be obtained in a full evaluation. A negative RBS score as obtained in some cases would indicate that risks outweigh benefits and therefore the activity would be unlikely to obtain regulatory approval.

Applicability of the risk benefit framework in South Africa

The example above applied the methodology for risk-benefit assessment to a GM crop release in South Africa. Therefore it is appropriate to determine how the methodology might be formally incorporated into the South African regulatory system.

In South Africa, GMO releases are regulated under the GMO Act (Act 15 of 1997) as amended by the GMO Amendment Act (Act 23 of 2006). New Regulations were published in 2010 (South African Department of Agriculture, Forestry and Fisheries 2010). A scientific advisory committee evaluates a dossier provided by an applicant under the Act, and provides feedback to an Executive Council, where decisions are made. The Executive Council consists of representatives from a number of relevant government departments. The Act is administered by the National Department of Agriculture, Forestry and Fisheries. The major purpose of the amendments to

Table 8 Summary risk-benefit assessments of other events

GMO	ES	AS	FS	HS	SS	RBS
Atlantic salmon with increased growth rate for fish farming in Europe[a] (Le Curieux-Belfond et al. 2009)	−89.3	3.7	4.0	0	9	−71
Ventria oral rehydration rice with lactoferrin and lysozyme for commercial confined production in Peru (assumed no wild rice relatives) or Burkina Faso (sexually compatible wild relatives) (Zavaleta et al. 2007)	0 (Peru)	−10.8	0.4	8.6	3.8	2.0 (Peru)
	−4.2 (Burkina Faso)	−10.8	0.4	8.6	3.8	−2.2 (Burkina Faso)
Open field release in Malaysia of male *Aedes aegypti* mosquitoes with a lethal trait to combat dengue fever (Beech et al. 2009)	0.5	0	0	22.5	4.4	27.4

[a] The score takes into account a high probability of escape from containment

the Act made in 2006 was to incorporate additional requirements of the Cartagena Protocol on Biosafety.

Although GMOs are primarily handled under the GMO Act, their regulation is also provided for under the National Environmental Management Biodiversity Act (NEMBA) (Act 10 of 2004). This Act makes provision that the Minister for Environment Affairs may require an environmental assessment if there is a threat to any indigenous species or the environment. The Environmental Impact Assessment Regulations (South African Department of Environmental Affairs 2010) specifically states that the release of GMOs into the environment requires an environmental authorization. A basic assessment carried out according to the regulations would detail a range of impacts, both positive and negative.

Morris and Koch (2002) pointed out that African regulators have tended to include a risk-benefit analysis in their decision making. While this trend was certainly noted in the early days of the South African introduction of GMOs, the regulatory processes appear to have shifted to a more conservative approach in recent years, no doubt influenced by the precautionary approach of the CPB. South Africa is moving towards full implementation of the CPB. This could also reflect a shift towards the very conservative or even preventative approach adopted by many African countries (Morris 2008), which is hampering the adoption of GM technology on the African continent as a whole.

A recent publication of the Academy of Science of South Africa (2010) states that "in order to effectively evaluate GM crops, an acknowledgement of their potential benefits must be made in addition to an evaluation of the potential damage to human health and the environment". Thus there are already influential voices urging the introduction of risk-benefit analysis, while at the same time expressing concern that "the South African authorities appear to be becoming more conservative and less willing to grant permits".

The GMO Act and Regulations do not currently make specific provision for consideration of benefits, except perhaps in the case of socio-economic considerations, where the term "impact" is used rather than "risk". The reviews conducted by the Advisory Committee follow a standard format that makes no reference to benefits. Up till now, the Executive Council has not produced any decision documents to support their decisions to approve or reject applications under the GMO Act, hence there is no written indication whether benefits are considered in any way. Anecdotal evidence suggests that the process of decision making in the Executive Council is quite informal, and that individual members will bring up matters of concern based on their mandates. If the Council feels that the risk can be managed and that there are benefits, then they would normally grant approval.

In discussions with members of the Executive Council and the office of the Registrar of the GMO Act, it appeared that consideration of benefits could be more formally incorporated into the current regulatory procedures without requiring changes in legislation. There was some enthusiasm amongst people involved in the regulatory processes regarding

the adoption of a risk-benefit methodology as proposed in this paper, particularly since it would provide a more transparent framework, could bring focus to the decision making process and could facilitate the process of public consultation and stakeholder engagement.

Some current constraints that would need to be addressed to facilitate the adoption of the methodology included:

(1) The lack of an initial framing step in the South African process, whereby agreement could be reached on the issues at stake.
(2) The lack of any mechanism to decide up front on the application of a weighting factor to individual scores.
(3) The need for improved documentation to support the allocated scores.

Conclusions

In this paper, a new decision support tool for semi-quantitative risk-benefit analysis is proposed. This is intended as a simple methodology that would be especially applicable to regulators in developing countries with limited expertise and facilities. Its applicability in the South African regulatory system is discussed. The South African system is taken purely as an example to illustrate some of the complexities that may be involved in introducing a methodology of this nature.

In various parts of the world, there are increasing calls for risk-benefit analysis to form an integral part of the GMO regulatory processes. In many cases this may require an amendment of legislation. The CPB has resulted in the PP being embedded in much current and new legislation in countries that have ratified or acceded to the Protocol. The inclusion of a benefit component would cause no inherent conflict with the CPB, but requires a change in mindset amongst regulators.

It is to be hoped that the provision of a relatively simple tool to facilitate risk-benefit analysis, as proposed in this paper, will support and accelerate the introduction of consideration of benefit as well as risk. The availability of a well-structured decision support tool can also support risk-benefit communication, and hopefully assist in restoring trust between regulators, scientists, industry and the public.

Only through this type of intervention will countries start to move away from the conservative risk-oriented approaches that are preventing them from reaping the benefits of GM technology.

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References

Academy of Science of South Africa (2010) GMOs for African agriculture: challenges and opportunities. Workshop proceedings report. ISBN 978-0-9814159-7-0. http://www.assaf.org.za/?p=2305. Accessed 10 Aug 2010

Amin L, Jahi JM, Nor AR, Osman M, Mahadi NM (2007) Public acceptance of modern biotechnology. Asia Pac J Mol Biol Biotechnol 15(2):39–51

Beech CJ, Nagaraju J, Vasan SS, Rose RI, Othman RY, Pillai V, Saraswathy TS (2009) Risk analysis of a hypothetical open field release of a self-limiting transgenic *Aedes aegypti* mosquito strain to combat dengue. Asia Pac J Mol Biol Biotechnol 17(3):99–111

Bermúdez Muñoz S, Víquez Camacho M (2010) Valoración ambiental preliminary del riesgo-beneficio de la liberación de una semilla de arroz genéticamente modificada. Tecnol en Marcha 23(1):3–8

Conner AJ, Glare TR, Nap P-J (2003) The release of genetically modified organisms into the environment. Part II. Overview of ecological risk assessment. Plant J 33:19–46

Costa-Font J, Mossialos E, Rudisill C (2009) Optimism and the perceptions of new risks. J Risk Res 12(1):27–41

Craig W, Tepfer M, Degrassi G, Ripandelli D (2008) An overview of general features of risk assessments of genetically modified crops. Euphytica 164:853–880

Dawe D, Unnevehr L (2007) Crop case study: GMO golden rice in Asia with enhanced vitamin A benefits for consumers. AgBioForum 10(3):154–160

Drobnik J (2008) Time to relax GMO regulation in Europe. Plant Cell Tiss Organ Cult 94:235–238

EFSA (2005) Opinion of the scientific panel on genetically modified organisms on a request from the commission related to the notification (reference C/F/96/05.10) for the placing on the market of insect resistant genetically modified maize Bt11, for cultivation, feed and industrial processing, under Part C of directive 2001/18/EC from Syngenta Seeds. EFSA J 213:1-33. http://www.efsa.europa.eu/en/scdocs/doc/213.pdf. Accessed 10 Aug 2010

EFSA (2006) EFSA Colloquium 6: summary report on risk-benefit analysis for foods: methods and approaches 13–14 July 2006, p 20

EFSA Scientific Committee (2010) Guidance on human health risk-benefit assessment of food. EFSA J 8(7):1673

(41 pp). doi:10:2093/j.efsa.2010.1673. Available online: www.efsa.europa.eu

Espinoza-Esquivel AM, Arrieta-Espinoza G (2007) A multidisciplinary approach directed towards the commercial release of transgenic herbicide-tolerant rice in Costa Rica. Transgenic Res 16:541–555

Falck-Zepeda JB (2009) Socio-economic considerations, article 26.1 of the Cartagena protocol on biosafety: what are the issues and what is at stake? AgBioForum 12(1):90–107

Giannakas K, Yiannaka A (2008) Market and welfare effects of second-generation, consumer-oriented GM products. Am J Agr Econ 90:152–171

Gómez-Barbero M, Rodríguez-Cerezo E (2006) Economic impact of dominant GM crops worldwide: a review. European Commission Joint Research Centre—Institute for Prospective Technological Studies Technical Report Series. EUR 2257 EN. ISBN 92-79-03879-6

Hill RA, Sendashonga C (2003) General principles for risk assessment of living modified organisms: Lessons from chemical risk assessment. Environ Biosafety Res 2:81–88

Huang J, Hu R, Rozelle S, Pray C (2006) Genetically modified Rice, yields and pesticides: Assessing farm-level productivity and health effects in China. Stanford University Working Paper. http://iis-db.stanford.edu/pubs/21625/GMrice_and_productivityl_25_Sept_2006_workingpaper.pdf. Accessed 10 Aug 2010

Ijas A, Kuitunen MT, Jalava K (2010) Developing the RIAM method (rapid impact assessment matrix) in the context of impact significance assessment. Environ Impact Assess Rev 30:82–89

James C (2009) Global status of Biotech/GM Crops:2009. The first fourteen years: 2006–2009. ISAAA Brief 41

Kostandini G, Mills BF, Omamo SW, Wood S (2009) Ex ante analysis of the benefits of transgenic drought tolerance research on cereal crops in low-income countries. Agric Econ 40:477–492

Kuiper HA, Davies HV (2010) The SAFE FOODS risk analysis framework suitable for GMOs? A case study. Food Control. doi:10.1016/j.foodcont.2010.02.011

Kuitunen M, Jalava K, Hirvonen K (2008) Testing the usability of the rapid impact assessment matrix (RIAM) method for comparison of EIA and SEA results. Environ Impact Assess Rev 28:312–320

Laursen L (2010) How green biotech turned white and blue. Nat Biotechnol 28(5):393–395

Le Curieux-Belfond O, Vandelac L, Caron J, Séralini G-É (2009) Factors to consider before production and commercialization of aquatic genetically modified organisms: the case of transgenic salmon. Environ Sci Policy 12:170–189

Linacre NA, Falck-Zepeda J, Komen J, MacLaren D (2006a) Risk assessment and management of genetically modified organisms under Australia's gene technology act: considerations for regulatory development. Asian Biotechnol Dev Rev 8(3):1–16

Linacre NA, Gaskell J, Rosegrant MW, Falck-Zepeda J, Quemada H, Halsey M, Birner R (2006b) Strategic environmental assessments for genetically modified organisms. Impact Assess Proj Apprais 24(1):35–43

Morris EJ (2008) The Cartagena protocol: implications for regional trade and technology development in Africa. Dev Policy Rev 26(1):29–57

Morris EJ, Koch M (2002) Biosafety of genetically modified crops—an African perspective. AgBiotechNet, vol 4, December, ABN 102

Morris SH, Spillane C (2008) GM directive deficiencies in the European Union. EMBO Rep 9(6):500–504

Morris EJ, van Rensburg JBJ, Hoffmann JA, Lazarus P (2005) Good regulatory practices for developing countries: lessons learned in South Africa from an appeal under the GMO Act. ICABR Int Conf Agric Biotechnol. http://www.economia.uniroma2.it/conferenze/icabr2005/papers/Morris_Jane_paper.pdf. Accessed 10 Aug 2010

Palou A, Pico C, Keijer J (2009) Integration of risk and benefit analysis—the window of benefit as a new tool? Crit Rev Food Sci Nutr 49:670–680

Pastakia CMR, Jensen A (1998) The rapid impact assessment matrix (RIAM) for EIA. Environ Impact Assess Rev 18:461–482

Qaim R (2009) The economics of genetically modified crops. Annu Rev Resour Econ 1:665–693

Ronald PC, Adamchak RW (2008) Tomorrow's table: organic farming, genetics and the future of food, p 226. Oxford University Press. ISBN 978-0-19-530175-5

Secretariat of the Convention on Biological Diversity (2000) Cartagena protocol on biosafety to the convention on biological diversity: text and annexes. Secretariat of the Convention on Biological Diversity, Montreal

Slovic P (1987) Perception of risk. Science 236:280–286

South African Department of Agriculture, Forestry and Fisheries (2010) Genetically Modified Organisms Act (1997) Regulations. South African Government Gazette 32966: 5–13. 26 Feb 2010

South African Department of Environmental Affairs (2010) National Environmental Management Act (Act No 107 of 1998) Environmental Impact Assessment Regulations. South African Government Gazette 33306:3–200

Starr C (1969) Social benefit versus technological risk. Science 165:1232–1238

Swart JAA, Jiang J, Ho P (2007–2008) Risk perceptions and GM crops: the case of China. Tailor Biotechnol 3(3):11–28

Tennøy A, Kværner K, Gjerstad KI (2006) Uncertainty in environmental impact assessment predictions: the need for better communication and more transparency. Impact Assess Project Appraisal 24(1):45–56

UNCED (1992) Rio declaration on environment and development. http://www.un.org/documents/ga/conf151/aconf15126-1annex1.htm. Accessed 10 Aug 2010

Vlek C (2010) Judicious management of uncertain risks: I. Developments and criticisms of risk analysis and precautionary reasoning. J Risk Res 13(4):517–543

Warwick SI, Beckie HJ, Hall LM (2009) Gene flow, invasiveness and ecological impact of genetically modified crops. The year in evolutionary biology 2009. Ann NY Acad Sci 1168:72–99

Wingspread (1998) Wingspread statement on the precautionary principle. Rachel's environment and health weekly 586,

2 pp. http://www.rachel.org/en/node/3850. Accessed 10 Aug 2010

Winter G (2008) Nature protection and the introduction into the environment of genetically modified organisms: risk analysis in EC multilevel governance. RECIEL 17(2):205–220

Zavaleta N, Figueroa D, Rivera J, Sánchez J, Alfaro S, Lönnerdal B (2007) Efficacy of rice-based oral rehydration solution containing recombinant human lactoferrin and lysozyme in Peruvian children with acute diarrhea. J Pediatric Gastroenterol Nutr 44:258–264