Chapter 35

Biosafety Forecast Service: The Precautionary Approach in practical Biosafety

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'In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. 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.'

(Principle 15, Rio Declaration on Environment and Development)

Biosafety Forecast Service (BFS)

The Precautionary Approach and the BFS

The Cartagena Protocol on Biosafety is an international treaty regulating primarily the transboundary movement of living modified organisms (LMOs). The Protocol, adopted as a supplement to the Convention of Biological Diversity, seeks to protect biological diversity from the potential risks posed by LMOs resulting from modern biotechnology. The Biosafety Protocol emphasizes the precautionary approach, allowing a country to reject or place restrictions on the importation or release of an LMO when the science on the potential benefits and hazards to human health and the environment is uncertain.

The Biosafety Forecast Service (BFS), a research-based risk identification and analysis project, was conceived with the principles of the Biosafety Protocol and the precautionary approach in mind. The Service is designed to support scientific risk assessment and holistic decision making by countries meeting their obligations under the Protocol, identifying areas of scientific uncertainty (Box 35.1) in applications for the release of LMOs (and more generally, genetically modified organisms, GMOs) as food, feed and medicine into the environment. It is also intended to assist regulatory authorities, non-governmental organizations (NGOs), civil society leaders, and citizens operating within their National Biosafety Frameworks.

Decisions taken on LMOs by countries party to the Biosafety Protocol should be preceded by a scientific risk assessment. They may also take into account socio-economic considerations, especially with regard to indigenous and local communities. The BFS is planned to support decision-making and the evaluation of LMO applications through both guidance for scientific risk assessment and the analysis of potential socio-economic and legal impacts.

Box 35.1 Examples of areas of scientific uncertainty

The identification of areas of scientific uncertainty permits the recognition of fields of biosafety where more research is needed. A few examples of these areas include:

Effect of novel RNAs.

- Gene silencing caused by RNA interference (RNAi)

Post-translational modification.
- In vitro studies using the in-planta produced protein in comparison to the bacterial version.
- Detection of minor variants.

Effects on non-target species.
- For bio-pesticides.
- For pharma crops.

Scientific risk assessment
A scientific risk assessment is based on risk identification, which may be customized on a case-by-case basis depending on the modified organism, its modification or its intended application. The BFS produces briefings on generic scientific risk issues as well as case studies that include custom assessments.

Risk identification can include aspects of an LMO from its production to its release into the environment and its use as food or feed. It includes aspects such as the molecular biology of the modification, genetic stability and effects of out-crossing and potential environmental and food hazards (Box 35.2).

Box 35.2 Examples of risk identification issues

Molecular issues include identifying and characterizing changes to:
- the genome, e.g. insertions, mobile elements, DNA processing sites, regulatory DNA sequences and introns;
- the transcriptome, e.g. novel mRNA molecules, silencing effects and regulatory RNA molecules;
- the proteome, e.g. novel polypeptides, modifications, and structures, unanticipated loss of a protein.

Genetic issues include:
- stability of the modification, gene and gene product across tissues and over generations;
- stability of the modification, gene and gene product in hybrids;
- impact of horizontal gene transfer.

Food hazard issues include:
- equivalence of modified and conventional counterparts;
- analysis of novel products and metabolites/catabolites;
- potential allergens, toxins, anti-nutrients, carcinogens, and co-carcinogens;
- uptake of DNA and other products specific to the GMO through food;
- factors undermining the sustainability of alleged benefits.

Environmental hazards include:
- horizontal gene transfer in the environment;
- effects of co-technologies (e.g. herbicides) used with the GMO;

- impacts on biodiversity;
- factors undermining the sustainability of alleged benefits.

Analysis of potential socio-economic impacts
An evaluation of socio-economic impacts covers a wide range of issues, often specific to an area, organism, or an organism's intended application. The BFS generates briefings on general socio-economic issues (Box 35.3) as well as case studies that include customized assessments.

Box 35.3 Examples of socio-economic issues
Socio-economic issues are diverse; they may include:

- the economic costs and benefits associated with the production and use of the LMO/GMO (including an assessment of the impacts on market access);
- the resource demands of adequate monitoring and containment of the LMO/GMO;
- the compatibility of the management procedures required by LMOs/GMOs with valued socio-cultural practices and resources;
- the socio-economic impacts of GMO-related farming regimes (e.g. changes related to intellectual property, co-practices, capital inputs, size of functional landholding), especially on indigenous and local communities;
- the socio-economic implications arising in the event of a loss of biodiversity, (e.g. through introgression of transgenes into traditionally important species or landraces);
- the potential impacts of the LMO/GMO on the rights of indigenous communities.

Analysis of legal implications
Any decision taken on LMOs should consider both domestic and international legal obligations, including those concerned with intellectual property protection and biodiversity.
An analysis of legal implications covers the conditions and constraints that may arise in conjunction with the purchase and use of LMOs. It also assesses state-level rights and obligations under international agreements, such as the Convention on Biological Diversity and the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

The Biosafety Assessment Tool (BAT)

Context
A comprehensive survey of the resources already freely available to support decision making and risk assessment processes for GMOs was conducted in November and December 2004 by the team of the Biosafety Forecast Service. This survey revealed that existing resources mainly comprised databases of highly technical literature for specialists; comprehensive, but not quality assured, databases associated with distribution services; and decision-tree formats providing little or no background support for the user.

The BFS is purposefully different to existing services in several important ways. First, it will be quality assured. Most of the content development for the BFS involves work at the leading edge

of the research literature. New knowledge is also produced by the team, to meet the highest international standards of peer review. For example, two technical summaries have already been published, one on monitoring GMOs and one evaluating designs of experiments purporting to assess the impacts of horizontal gene transfer.

Second, the BFS goes beyond simply providing summaries of risk issues and reviews of technical literature. To allow users to make their own interpretations of the information provided by applicants and regulatory agencies, the BFS is developing the Biosafety Assessment Tool, also called BAT.

BAT: The tool
The BAT will be a free-to-the-public electronic resource, designed as a practical tool for the risk assessment of GMO applications for food, feed, medicine, or environmental release. By using the BAT, policy and regulatory officials in government, non-governmental organizations (NGOs), citizens, and researchers will be able to customize biosafety information from the elite scientific and technical literature and apply it to their own risk assessments, or to evaluations of assessments done by others. It will help both the identification of relevant risk issues and assist with the evaluation of technical information provided in GMO import/release applications. Unlike a decision-tree approach that leads to a certain conclusion based on an analysis 'behind-the-scenes', the BAT is designed to make explicit the connection between the actual data supplied to regulatory authorities (e.g. by applicants) and considerations of risk so that the user can learn to recognize uncertainties in the evaluation of GMOs.

The aim is to make it possible for a user to construct a comprehensive and context-specific assessment of the technical information, as well as to identify what additional issues or uncertainties should be addressed by either regulatory authorities or the applicant.
The BAT will not only support the writing of scientific risk assessments but also assessments related to the socio-economic impacts. This emphasizes the holistic and independent approach of this tool. The tool will not tell the user whether to accept or reject a GMO; rather, it will assist the user to carry out GMO risk assessment and holistic decision making.

The organization of the BAT
The information within the BAT is organized as three different 'gates'. These gates have been customized to the needs of different users, or of the same user at different stages of risk evaluation.

Gate 1. Practical Assessment
Gate 1 will serve those prepared to assemble a final assessment of an application. The information in this section will be structured to reflect the organization of a typical application. It will explain the terms used in applications and the information that is, or should be, provided by the applicant.

Gate 2. Risk Assessment Guides
Gate 2 is based on a series of 'guides' designed to provide a comprehensive view of GMOs from production to release (Table 35.1). It could be used to complete an assessment or to gain a broad overview of GMOs and their implications. This Gate provides the rationale and references for the recommendations in Gate 1.

The guides that form part of this gate provide a more holistic view than the information displayed in Gate 1. These guides will provide information to assist decision makers and citizens with their

consideration of their own environmental, social, political, and economic context as well as scientific risk.

Table 35.1. Description of guides.

Guide	Description
GMO: The basics	The aim of this guide is to describe and explain the main scientific concepts used in applications and assessments. This guide will serve as a primer for all other guides.
GMO from DNA to insert	The aim of this guide is to suggest what could be considered in the assessment of the molecular characterization of a GMO. This will include the description of the risk spectrum of the transgene and the event.
GMO from protein to trait	The aim of this guide is to describe the risks and considerations from the RNA to the protein level of the molecular characterization of a GMO. This will include description of the transcriptome and proteome.
GMO and human safety	The aim of this guide is to make an assessment pertinent to human health. Main components of this guide will include: compositional analysis, allergenicity data and toxicological studies.
GMO and environment	The aim of this guide is to describe the risks and considerations for the release of a GMO into the environment. This can include gene flow, weediness, containment, coexistence, and effects on non-target organisms.
GMO management and monitoring	The aim of this guide is to assess strategies to monitor or contain a GMO once it has been approved for use in human food or for release into the environment.
GMO regulatory and legal issues	The aim of this guide is to illustrate models of existing regulatory frameworks, and to introduce new initiatives.

Gate 3. Risk Assessment Checklist

Gate 3 takes the form of a 'checklist'. The information presented in the BAT will be organized in this gate according to questions that may need to be considered by decision makers. It will explain the significance of the questions and point to information that may help the decision maker to address these questions in relation to their own country. This section is recommended for users that have finished their risk assessment.

The development of the BAT

In order to provide a model for the construction of the BAT, the BFS team has conducted extensive risk assessment analyses on glyphosate resistant wheat and LY038, a GM corn also called High Lysine Corn (Box 35.4). These analyses were used to plan the BAT, covering the steps taken to evaluate each scientific study and the costs and benefits of the proposed policy decisions.

Box 35.4 LY038: A case study

In 2004 an application (A549) was submitted to the food safety authority for New Zealand and Australia (Food Standards Australia New Zealand – FSANZ) to allow the introduction of LY038 high lysine corn into the human food supply. The BFS team assessed this application in the form of two submissions* to FSANZ. These submissions have been used as a training tool for the BFS

team and as a source of case studies for the development of content for the Biosafety Assessment Tool (BAT).

LY038 is a genetically modified corn that accumulates lysine and free lysine in the grain. Free lysine and lysine metabolites accumulate to levels with no historical precedent in comparison to conventional corn, making LY038 one of the first nutritionally enhanced GM organisms that food safety approval has been sought for.

More than 15 studies were included in A549, ranging from the molecular characterization to bioinformatics and feeding studies. These studies were assessed to answer two main questions:

- Do the scientific data made available by the applicant conform to the best international standards?
- Was the safety assessment conducted using the best available science?

The scientific risk assessment was accompanied by an analysis of the potential costs and benefits of changing the food code to permit LY038 in the human food supply.

The first submission was made in February 2005, with the second released in June 2006. In the latest submission, 95 recommendations were made to FSANZ highlighting concerns mainly related to food hazards and the cost-benefit analysis.

To allow the submissions to be used as the basis for the development of the BAT, the team has customized them for a wider audience, using more accessible scientific language and adding a discussion of the process used to identify risk issues. The documents will be reconfigured as practical resources, outlining the steps taken in evaluating each scientific study and allowing BAT users to apply the same process to other pending applications.

*The submission to the Initial Assessment Draft for A549 and the submission to the Draft Assessment Report for A549 are freely available at http://www.inbi.canterbury.ac.nz/ly038.shtml

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As part of the testing and evaluation of the BAT, several prototypes have been developed and more are still to come. Each prototype has a specific feature to be tested in evaluation sessions. This allows us to optimize the tool for our users.

Prototype version 1

The first prototype of the BAT was designed to get feedback about the usefulness of the tool itself – the quality and relevance of its information; the level or difficulty of the information; the prototype's organization and style – and to assess the prototype's sensitivity to different country needs.

For this first version, an easy-to-handle format was preferred, highlighting content rather than sophisticated functionalities. Microsoft PowerPoint was chosen as the platform and Prototype version 1 was launched in August 2005. This prototype demonstrated the approach of the BAT and the kind of information that will be provided in its interactive format, prompting valuable feedback to aid future technical development.

Two venues for testing and evaluation were used (Box 35.5): the Solomon Islands Regional Biosafety Course held in Honiara, Solomon Islands and the Holistic Foundations for Assessment

and Regulation of Genetic Engineering and Genetically Modified Organisms international biosafety course held in Tromsø, Norway.

Overall, the feedback sessions reinforced the merit of the general approach of the BAT in providing easy-to-follow, holistic information from the world of biosafety research in a format useful to those producing risk assessments. Participants commented that the prototype version 1 content and visual aids clarified complex scientific ideas that had previously confused them, suggesting that the BAT had the potential to fill a need within the risk assessment community for authoritative yet accessible biosafety resources. The holistic nature of the prototype engaged participants with disparate specialized backgrounds.

Box 35.5 Evaluation sessions for Prototype version 1

Figure 35.1 Prototype version 1 of the BAT

The first focus group that provided feedback on Prototype version 1 (Fig. 35.1) was assembled at the Solomon Islands Regional Biosafety Course held in Honiara, Solomon Islands, in August, 2005.* Participants representing the private sector and different areas of the Solomon Islands public sector, non-governmental organizations and educators were brought together during this course to use the prototype. This version of the BAT was used by participants in a workshop to assess a fictional application (for a GM fruit) of the type that could be received under the Biosafety Protocol (Fig. 35.2).

A second focus group was assembled at the Holistic Foundations for Assessment and Regulation of Genetic Engineering and Genetically Modified Organisms international biosafety course, held in Tromsø, Norway in September 2005.

Figure 35.2 Evaluation of the Prototype version 1 of the BAT held in Honiara, Solomon Islands as part of the Solomon Islands Regional Biosafety Course

A day of client feedback on Prototype version 1 was conducted, again assessing the fictional GM application. This feedback session aimed to evaluate the conceptual basis of the BAT, its usefulness, and its requirements in terms of function and design. The pool of participants at these biosafety courses was identified as an ideal group of potential BAT users. Positive feedback was received on the prototype from these sessions, with constructive comments for the simplification, organization and expansion of the information within.

* A full report of this course can be found at
http://www.inbi.canterbury.ac.nz/news_biosafety_solomons.shtml

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Prototype version 2

The main concerns that emerged during the evaluation of Prototype version 1 included the organization of the information within the limitations of the PowerPoint programme. Prototype version 2 addresses this by using a web-based interface. This allows the introduction of features such as menus, structured pathways and a search engine. Further components have been designed for this new version, such as an interactive window and a toolbar (Box 35.6). It is important that the effectiveness of these innovations is tested in future feedback sessions.

Box 35.6 Prototype version 2 of the BAT

Prototype version 2 of the BAT was designed in a web-based format. The layout of the tool is divided into three parts:

- The toolbar includes several features, including search and map functions. It will also include features that will allow users to write and save comments, quotes and references and export the gathered information into other programs for further use (Fig. 3A).
- The main screen, where information will be displayed, allows navigation using active links (Fig. 3B).
- The interactive window displays additional information related to the content of the main screen. It also displays definitions of highlighted words included in the glossary (Fig. 3C).

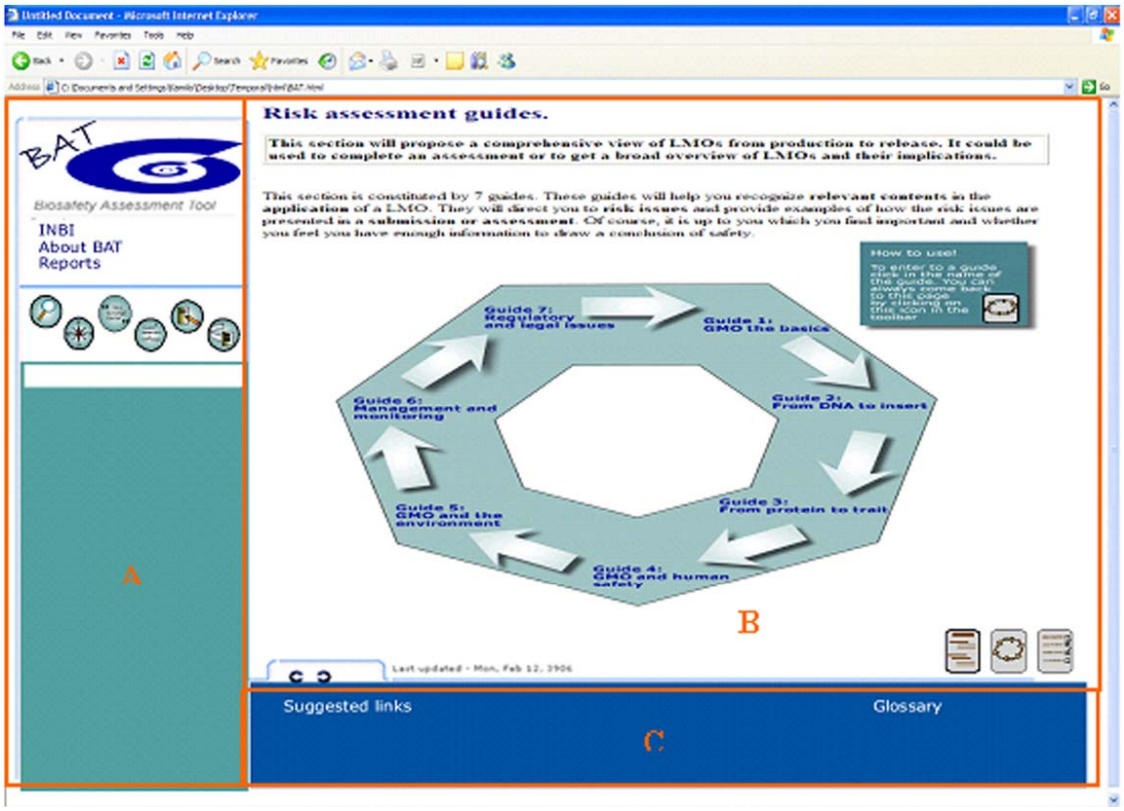

Fig 35.3 Layout of Prototype version 2. A)Toolbar B) Main screen C) Interactive window

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Prototype version 2 already has many features that will be released in the final version of the BAT. This version was first tested for its functionality and usability at the international Biosafety Course in Tromsø in August 2006 (Box 35.7). Other evaluation sessions are planned to take place in 2007.

Box 35.7 Evaluation session for Prototype version 2

Prototype version 2 was evaluated in three workshops on the molecular, health and environmental assessment of an application for the approval of LY038 corn (see Box 35.4). This evaluation session took place at the Holistic Foundations for Assessment and Regulation of Genetic Engineering and Genetically Modified Organisms international biosafety course, held in Tromsø, Norway in August 2006.

Feedback from this session was overwhelmingly positive.* Participants expressed their interest in the use of the BAT in a professional capacity, not only as a regulatory assessment tool but also as research database and teaching and training resource.

Figure 35.4 Participants in the evaluation session of the Prototype version 2 of the BAT

* A full evaluation report can be found at http://www.inbi.canterbury.ac.nz/news_bat2006.shtml

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Conclusion

Following the principles of the Cartagena Protocol on Biosafety, the BFS aims to support countries in LMO assessment by providing a holistic approach to decision making. The BAT was born from discussions with NGOs, policy makers, regulators and, ordinary citizens from all over the world interested in contributing to a robust biosafety framework in their countries. The technical nature of scientific risk assessment and the limited distribution of information mean that there can be significant barriers to participation in GM decision making. It is hoped that the BAT will help reduce the elitism of scientific risk assessment, promoting a more informed and critical analysis of GMOs.

The Biosafety Assessment Tool is practical. Users are assisted to form an assessment based on issues that they find relevant. Unlike decision-tree approaches, issues of risk will not be set and pre-ordered, but identified and evaluated by the user for their specific context.

The development funding for the BFS is scheduled to end in 2007. However, the Tool is a living resource. It will need constant attention and updating to maintain it at the leading edge of risk identification and social change.

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