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Proceedings of the Workshop on Risk Assessment in Biosafety

(San Jose, 26th February to 2nd March 2013)

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Proceedings of the Workshop on Risk Assessment in Biosafety
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Inter-American Institute for Cooperation on Agriculture (IICA)

UNEP-GEF Project "Implementation of a National Biosafety Framework for Costa Rica" (UNEP-GEF-CR)

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Foreword

Biotechnology and biosafety have a key role to play in the development of modern agriculture. Biotechnology furnishes technological tools, and biosafety provides regulatory frameworks to ensure that those tools are used correctly. Based on this principle, IICA carries out biotechnology activities focused on institution building, capacity development and communication in aid of the agriculture of its member countries.

In the area of institution building, IICA responded to the countries' request for the creation of the Central American Initiative on Biotechnology and Biosafety (ICABB), following biotechnology and biosafety efforts in other regions of the hemisphere such as the North American Biotechnology Initiative (NABI) and the G5 of the Southern Agricultural Council (CAS). The ICABB was created to consolidate biotechnology and biosafety in an integrated and responsible way in the countries of the Central American region.

IICA assumed the commitment of developing technical capabilities in biotechnology and biosafety in its member countries in a responsible and transparent way, incorporating the subject into its lines of work. Under these two strategic lines of action, training and upgrading courses are essential to ensure that biotechnology is used effectively in agriculture. The course on "**Risk Analysis in Biosafety,**" comprised of theoretical components and field visits, is an example of the way in which IICA addresses the subject, and could be used as a model in other regions of the hemisphere.

The course generated useful knowledge and information for regulators, academics, developers, producers, and consumers to draw on; hence the importance of capitalizing on the experience.

IICA thanks Agriculture and Agri-Food Canada (AAFC), as well as UNEP-GEF Costa Rica, for their support for the organization of the course. The Institute also wishes to acknowledge the contribution made by the developers, who allowed biosafety regulators from a number of countries to learn about original genetic modification events first hand. We hope that such events will be released more frequently in the future, with technical knowledge being used to make the appropriate biosafety decisions.

Víctor Villalobos
IICA Director General

Proceedings of the Workshop on Risk Assessment in Biosafety

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Introduction

Support for the development of technical capabilities in the field of biosafety is an important aspect of the technological and economic development of the Latin American and Caribbean (LAC) countries. For this reason, institutions such as IICA, UNEP-GEF, AAFC, USDA, etc., promote and support training activities for specific groups.

In response to a formal request from the Central American countries, IICA facilitated the creation of the Central American Initiative on Biotechnology and Biosafety (ICABB). During the workshops held to discuss the design of the ICABB, risk assessment was identified as one of the critical issues with which the region's biotechnology authorities needed assistance.

Based on this finding, AAFC, IICA and the UNEP-GEF Costa Rica Project decided to sponsor a five-day workshop comprised of a series of papers on specific aspects of risk assessment presented by renowned experts, opportunities for the participants to discuss the issues raised, and a field visit to observe examples of biosafety in non-conventional genetically modified organisms (GMOs) such as GM salmon and GM pineapple.

This document contains a summary of the workshop. The expert presentations are divided into the following sections: General aspects of risk assessment (Section 1), Practical examples of risk assessment in crop farming and forestry (Section 2), Low Level Presence (Section 3), Risk assessment in animals (Section 4), and Risk assessment in the environment and health sectors (Section 5). Comments about the ICABB are also included (Section 6). The final section provides an overview of the workshop and contains the list of participants and the program (Section 7).

Published in both English and Spanish, this document is targeted at a wide audience interested in biotechnology and biosafety. It offers useful technical information and details of experts on the subject.

Section 1: Basics of Risk Assessment

1.1. An introduction to the risk assessment of transgenic crops: Canada's experience[1]

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Traditionally, plant breeders have often relied on intensive effort with only incremental gain to develop and improve crop varieties. Using the tools of modern biotechnology, plant breeders have a new range of precise techniques that can assist them in introducing traits that may not be possible or as rapidly achievable with more conventional breeding techniques. In Canada, there was a recognition that while genetic engineering could produce products that could pose a risk to human and animal health and the environment, the issue was not the technology used but, rather, the product that was produced. For example, plant breeders can use mutation breeding to produce crop varieties that are tolerant to broad spectrum herbicides or change the composition of an oilseed like soybean by elevating the oleic acid levels. As a consequence, in Canada, the decision was made to regulate all plant products with truly "novel" traits (plants with novel traits or PNTs) no matter how they are produced. A PNT is subject to a pre-market risk assessment prior to marketing or environmental release. For the purposes of this paper, the discussion will be confined to transgenic plants, since that is the area of interest for most countries. It is worth noting, however, that these principles are applied to all PNTs in Canada.

Risk assessment is a key step in determining the safety of PNTs, which include transgenic plants. Risk assessment, however, includes risk management strategies and risk communication in addition to risk assessment. The risk assessment is based on science and is applied case-by-case using scientifically sound and verifiable data. The objectives of a risk assessment of a transgenic plant for commercial release are not the same as those of scientific research. While both activities are hypothesis-driven forms of structured, empirical inquiry, the objective of the risk assessment is to address the relative safety of a product intended for release rather than an ongoing quest to enhance fundamental knowledge. By implication, if the risk assessment is to be relevant and suit the intended purpose, it will need to be completed in a timely manner and there may be some residual uncertainty in the analysis and questions not directly related to determining the relative safety of the PNT may remain unaddressed.

Risk management may be required as an outcome of the risk assessment to mitigate potential risks that have been identified or to address uncertainty. Risk management will often include non-scientific considerations, such as whether management measures are feasible, cost effective or socially acceptable.

[1] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/01%202013-02-26%20PMcDonald.pdf

Risk communication provides a mechanism for interchange among risk assessors, risk managers and other interested parties. Different countries will approach risk communication according to their needs and resources.

The environmental risk assessment of a transgenic plant involves the identification of potential hazards, an evaluation of the likelihood of the hazard occurring, along with a determination of potential exposure of the environment to the hazard, then determining whether this could result in harm. Hazard can be defined as a potential source of damage, and harm is considered to be the negative outcome from the hazard. Risk is the probability of whether harm will result.

Environmental risk assessment must consider the risk of a hazard leading to harm in terms of the potential exposure to the hazard in the environment. This relationship is usually expressed as:

Risk = Hazard x Exposure

This equation is useful when differentiating between the information requirements at different scales of release. For example, the information available for the release of a transgenic plant as a small-scale field trial is often quite limited, so in such situations risk is minimized by controlling the transgenic plant's environmental interactions by imposing terms and conditions that prevent pollen flow, dispersal of seed and vegetative matter and persistence in the environment after the trial is completed.

In Canada, environmental risk assessment is based on the concepts of familiarity and substantial equivalence. A risk assessment takes advantage of what is known about the biology and environmental interactions of the species that has been genetically engineered. In Canada, specific biology documents are prepared that cover the important aspects of the plant's biology, including reproductive biology, growth habit, agronomic management practices and environmental interactions. Generally, the risk assessment compares the transgenic plant to a closely related counterpart and any significant differences are identified during the risk assessment. The biology documents are useful to set the context for the environmental risk assessment and also to help identify potential pathways to harm, for example outcrossing of an herbicide-tolerant trait from the transgenic plant to a sexually compatible weed species, resulting in a weed that is more difficult or impossible to manage.

Substantial equivalence is a useful mechanism to contextualize the differences that occur between the transgenic plant and the counterpart cultivated species. For example, when considering a transgenic herbicide-tolerant canola, the risk assessment will consider whether the impact of the transgenic canola on biodiversity is substantially the same as the impact of the conventionally cultivated species, recognizing that the monoculture of canola has an impact on the environment. Similarly, the risk assessment will consider whether the impact of the expression of the new trait, for example a modified enzyme that confers herbicide tolerance, is substantially the same as the canola plant's other gene products, recognizing that some gene products of the plant may also have negative environmental impacts.

Risk assessments begin with problem formulation, also called hazard identification, to identify how the environment could be affected by the cultivation of the transgenic plant. Information will be used to determine effects on measurable aspects of the environment, usually called assessment endpoints that have been identified before beginning the risk assessment. Examples

of assessment endpoints are the relative abundance of pollinators or the composition of indicator plant species populations. Endpoints reflect what we are trying to protect and often reflect a societal consensus, for example the need to protect endangered species. Generally, the protection of biodiversity and human health, as it relates to exposure in the environment, are key protection goals of an environmental risk assessment of a transgenic plant. In Canada risk assessors are guided in the process by structuring the hazard identification phase around "five pillars." These are the transgenic plant's potential to:

- become a weed;
- outcross to related species with negative consequences;
- affect non-target species;
- become a plant pest;
- affect biodiversity.

During the evaluation, some considerations will be deemed not relevant to the assessment, but others will be used to derive specific "risk hypotheses" that guide the collection and evaluation of data. Because scientific knowledge derives from tests of hypotheses, not from proofs of hypotheses, it is not possible to prove that release of a transgenic plant presents no risk to the assessment endpoints. It is possible, however, to attain high confidence that release of the transgenic plant presents low risk ("is safe") by rigorous tests of hypotheses that predict no adverse effects on the assessment endpoints (Raybould, 2006).

Since those conducting the risk assessment generally have formal scientific training, the separation between the types of inquiry that occur with curiosity-driven research and the structured but more limited scope of inquiry that occurs while conducting a risk assessment can be problematic. In countries that rely on arm's length scientific advisory boards rather than full time regulators to undertake risk assessments of transgenic plants, this difficulty may be more prevalent, particularly if the expert panels are also staffed with those conducting biosafety research. Regulators often speak of "need to know" *vs*. "nice to know" to help differentiate between questions driven by scientific curiosity from those that are necessary to address the risk assessment. In addition, the information that can usefully support a risk assessment for a product may include data that does not necessarily achieve the usual standards for a peer reviewed scientific publication, such as information from grower groups, agriculture extension personnel, and grower experiences. It is important to establish before the risk assessment what standard of proof is required and determine how evidence will be weighed. More data will not necessarily add more precision and unless properly focused more data may in fact create more uncertainty.

Risk assessment is generally central to the regulation of transgenic plants and policy considerations will inform all steps. These will include the determination of protection goals and endpoints, the implementation of risk management strategies, the determination of acceptable risk and strategies for engaging stakeholders, including the public. Risk assessment principles are common, and useful lessons can be gleaned from how countries with mature, functioning regulatory programs for transgenic plants have implemented these principles. Despite sometimes conflicting views, countries that have implemented functioning regulatory systems based on sound scientific principles have been successful in providing routes to commercialization of transgenic crops that address any potential risks to environmental, human and animal health, while giving producers access to a wider range of management tools.

Reference

Raybould, A. 2006. Problem formulation and hypothesis testing for environmental risk assessments of genetically modified crops. Environ. Biosafety Res. 5: 119-125.

1.2. Problem Formulation[2]

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What is problem formulation?
Problem formulation is a method of developing relevant questions for risk assessment (RA) as well as a plan to respond to those questions. It is a method used for focusing on aspects that require more attention and protection.

Focusing on problem formulation prevents the collection of unnecessary information for a RA, which streamlines the process. Consequently, RA becomes more efficient, less costly and more transparent, since it comprises the exact information sought and the reason why it is sought.

How does problem formulation fit within RA?

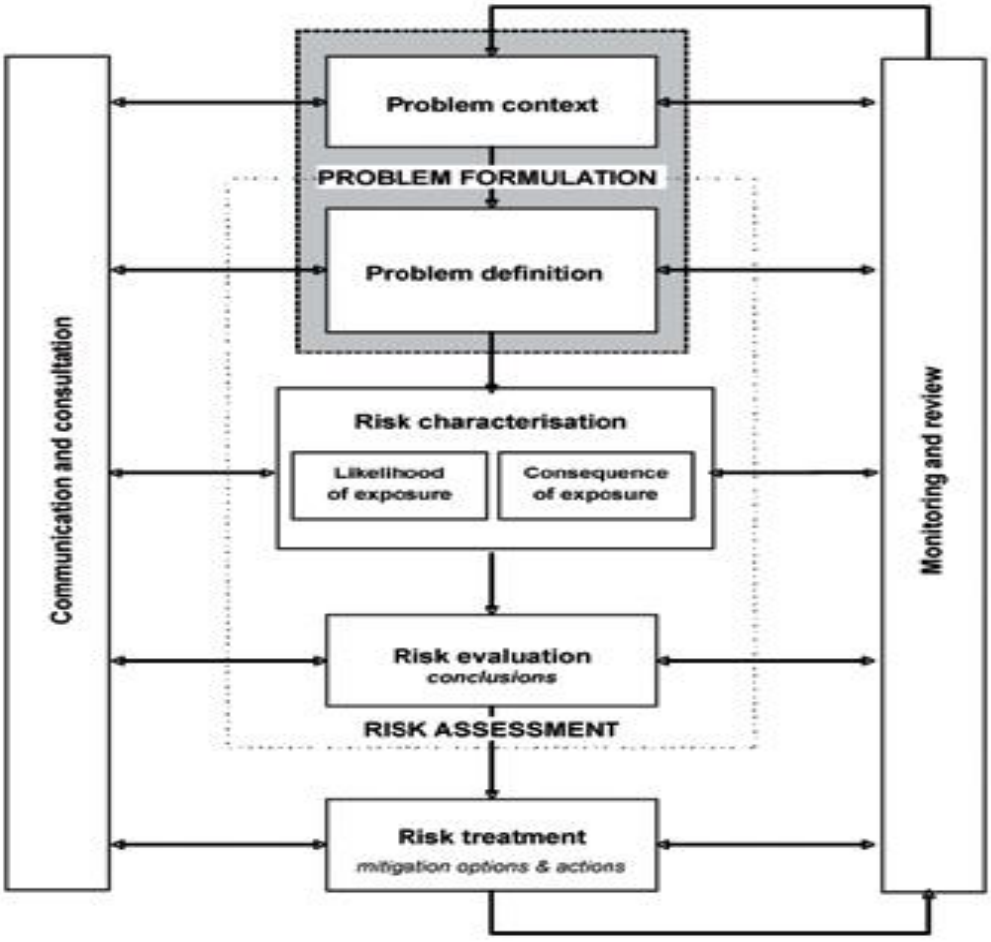

Figure 1. Problem formulation in risk assessment (Wolt *et al.* 2012)

[2] Full presentation is available at
http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/02%202013-02-26%20MAraya.pdf

What are the main elements of the problem formulation approach?

1. Identify elements that require protection.
2. Formulate scenarios that might affect the "elements of interest" identified.
3. Develop a hypothesis that can be used to determine whether the risk may occur.

What are the phases of problem formulation?

- General context of the problem:

An activity that establishes the parameters for risk assessment, taking into account the protection goals, the scope, the endpoints of the assessment and the methodologies. The objective of this phase is for the individual who conducts the risk assessment to move from very general environmental concerns to more specific and measurable aspects.

- Defining the problem:

Refers to an activity that involves identification of significant risks that require a specific assessment plan. It identifies the information necessary for characterizing the risk and methods to obtain that information.

The main objective of this phase is to transform general concerns identified in the preceding stage (context of the problem) into a series of risk hypotheses or case studies that can be verified.

Alan Gray sums up the problem formulation approach in four key questions:

Question	Stage in the PF approach
1. What must be protected? What do we NOT want to see harmed?	Identify assessment endpoints from protection goals
2) Can we envision a way in which the thing we want to protect may be harmed?	Trace pathways to danger or harm Develop exposure scenarios
3) How can we assess whether it is likely to be harmed?	Formulate risk hypotheses and an action plan
4) Does it matter? What is the context?	Re-analyze protection goals and the acceptability of the risk

Terminology-Glossary

-Protection goals: Objectives of environmental policies. Generally established in legislation and regulations.

-Assessment endpoints: Explicit expression of the environmental value that is susceptible to harm and may, at the same time, provide evidence of harm. It may be useful as a parameter of measurement.

References

Gray A. 2012. Problem Formulation in Environmental Risk Assessment for Genetically Modified Crops: A Practitioner's Approach. ICGEB. (collection of biosafety reviews). Available at http://www.icgeb.org/~bsafesrv/pdffiles/Col6_Gray.pdf

Section 2: Risk Assessment in Agriculture and Forestry

2.1. Risk assessment in agriculture: Experience in GM maize in Honduras[3]

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Honduras has advanced in the development of a regulatory framework for biotechnology and biosafety to enable the country to market GM crops to support its food security and agricultural development agenda. In 2003, the Government of Honduras authorized the planting of insect resistant (Bt) and herbicide resistant (RR) maize for commercial purposes on 2000 hectares of land, and ratified the Cartagena Protocol in 2008. As in other countries that have adopted it, this technology has spread readily in Honduras, with approximately 35,000 hectares of GM maize planted in 2012. This study describes the basic principles of risk assessment, which include the analysis, management and communication of risk. It also documents the regulatory frameworks governing biotechnology use in Honduras and other Central American countries, and analyzes the circumstances that led Honduras to become the only country in the Central American region to approve GM maize for seed production and planting for commercial purposes. Furthermore, this study presents the preliminary results of a study on the socioeconomic impact of Honduras' adoption of GM maize conducted by Universidad Zamorano, the International Food Policy Research Institute (IFPRI) and the University of California, Davis. It also explores the regulation of synthetic biology, "the second generation of genetic engineering," its applications and potential for education, and the regulatory challenges that the countries will face in the near future.

The planet is currently facing a "perfect storm," mostly due to a burgeoning population and environmental degradation. This will make it necessary to produce more biomass for food, bioenergy and materials using less land, water and fossil fuels, and at the same time cope with the effects of climate change. Maintaining the status quo, especially in the developing countries, is no longer an option; we must act now. The huge challenges we face are also great opportunities for change. The genomics revolution is already underway. The potential of the breakthroughs made in biotechnology and synthetic biology is enormous, but so are the challenges. Those responsible for regulating the use of such technologies must be mindful of their great potential but also of society's distrust of any new technology, especially when it is beyond their control. The future success of these technologies depends on regulatory policies being developed in a consistent and appropriate way, based on risk assessment rather than public opinion.

A presentation entitled "Risk Assessment in Agriculture" was given at a workshop held in Costa Rica by IICA and its collaborators in April 2013, targeted at regulators from Latin America. Taking Honduras as an example, the presentation focused on the risk assessment process as one of the three components of risk analysis (Fig. 2) and as a key element for decision-making.

[3] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/03%202013-02-26%20MMRoca.pdf

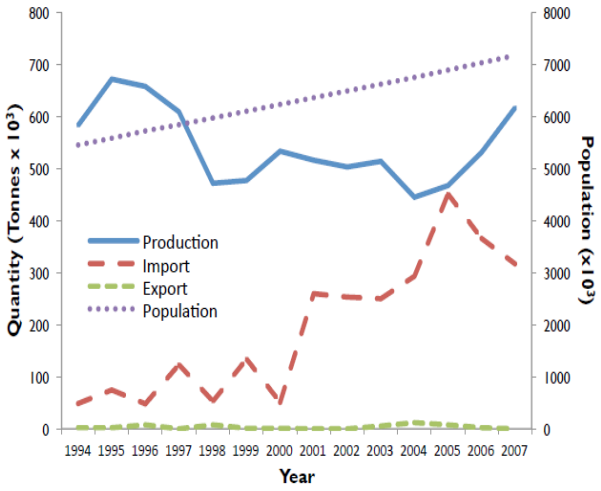


Figure 2. Honduras: Population and maize production, imports and exports (Source: FAO, 2011).

A country's decision to adopt or reject a new technology should be based on a series of parameters, including a cost-benefit analysis, a risk assessment and, lastly, a political decision that is in accordance with the country's legislation, agendas and priorities (Fig. 3), as well as international agreements.

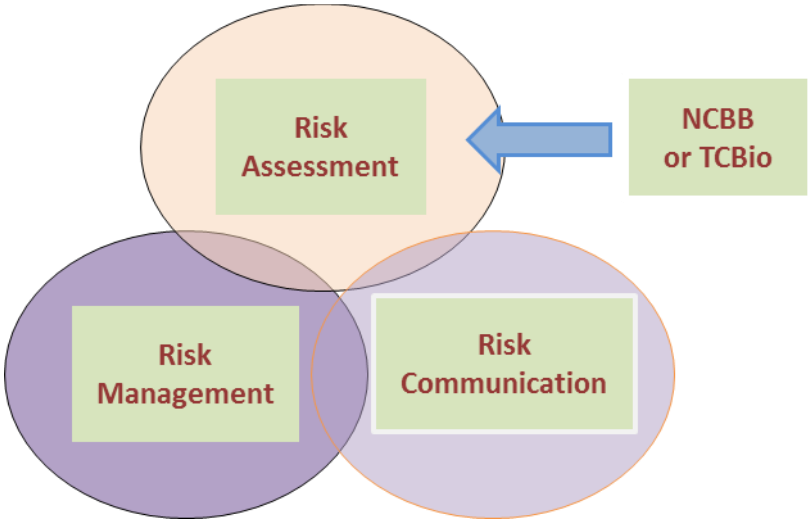
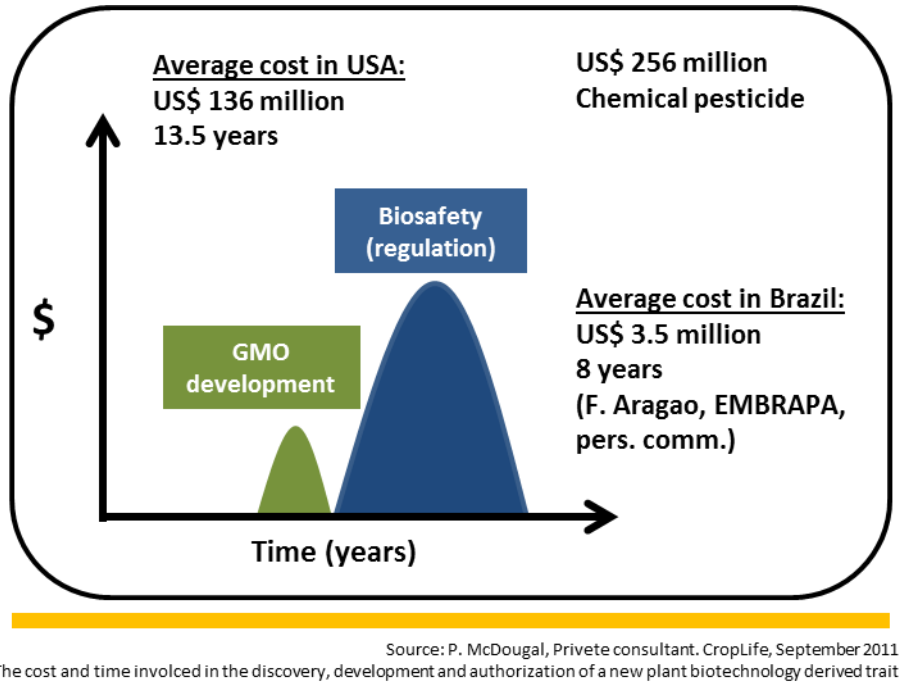


Figure 3. The three component of risk assessment.

The study analyzed the main reasons why the region has failed to harmonize its regulatory frameworks, These include: 1) different trends and political agendas; 2) a negative public perception of biotechnology; 3) lack of clear national biosafety strategies and confusion in the face of the complexity of interpreting and applying the Cartagena Protocol; 4) the countries' lack of technical capabilities for biosafety, specifically risk assessment; 5) other (very legitimate) priorities on the national agendas that take precedence over the development and application of regulatory frameworks governing biosafety.

The study highlighted the high cost and complexity of regulating biotechnology in agriculture compared with the cost of developing biotech products (Fig. 4), and the fact that the latter have been used safely used since they were first made commercially available in 1996. The study suggests that the high cost of regulation is a strong deterrent to the development of agricultural biotechnology, despite the fact that public institutions could use them to help solve local problems. It also affirms that the complexity of regulation delays the adoption of biotech products in developing countries, where they could make a significant contribution to agricultural production and food security programs.



Source: P. McDougal, Privete consultant. CropLife, September 2011
The cost and time involced in the discovery, development and authorization of a new plant biotechnology derived trait

Figure 4. Development of biotechnology *vs*. Costs for developing regulations

The Universidad Zamorano and its collaborators conducted two pieces of research (2008 and 2013) on the adoption of GM maize in Honduras, the preliminary results of which were presented as part of the case study. The results highlight the following trends: insect resistant (Bt) and herbicide resistant (RR) genetically improved varieties (hybrids) produce higher yields than local varieties; less insecticide is used to combat Lepidoptera pests; weed control is easier; and, farmers that used GM varieties had a higher net income, despite the high cost of GM seeds. The results confirm the same trends identified in similar studies carried out in other countries. The final results will be published officially at the end of 2013.

The presentation also referred to the progress made in the field of synthetic biology, which could revolutionize the development of new products such as pharmaceuticals, proteins for different uses, microorganisms and industrial enzymes, and also be used for bioremediation, pigments and biofuels, among others. Like biotechnology, synthetic biology will be regulated by the guidelines established for the member countries under the Cartagena Protocol. In addition to the potential of synthetic biology, countries face significant challenges in developing a consistent form of regulation that allows advances in science and technology to support education and society, while at the same time ensuring the safe use of technology and the fair distribution of its benefits.

2.2. Risk assessment in crops and forestry species[4]

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Agricultural biotechnology, which began with genetically modified (GM) grains such as maize and soybean, was subsequently applied to root crops and fruits. The groundwork is now being laid for the production of transgenic forest species. Public perception of transgenic crops now oscillates between acceptance and rejection, but in the case of genetically modified forest species it is negative. How did this come about? To what extent does this public perception (introduced after the risk management component) influence risk analysis and the other two components (risk assessment and risk management)?

Risk communication is often regarded as less important than risk assessment (Fig. 5) but it has a decisive (positive or negative) impact on the complexity and frequency of the latter, and on the scope and complexity of risk management. In the specific case of GM forest species, the public perception is based on opposition to biotechnology in general. Internet websites clearly inform public opinion, and that opinion is manifest in the public domain, undermining risk assessment and the bodies responsible for risk management or the agencies that carry out risk assessment.

Figure 5. The three components of risk assessment.

The risk assessment should focus only on the biological aspects of risk, while risk communication and management should address the different types of risks identified in the risk assessment and include all other hazards that originate from social perceptions. By integrating

[4] Full presentation is available at
http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/04%202013-02-26%20PPaes.pdf

the three components, the assessor is able to pinpoint the hazards that exist in the public's perception and provide communicators with information designed to ensure that the level of concern is in keeping with the risks actually detected. Integrating the information also means that the risk manager will not ask the risk assessor to perform unnecessary work; on the contrary, the assessor will furnish the technical data required for the correct management of the risks identified.

Risk assessment for forest species is no different from the work carried out with excellent results for transgenic crops. It comprises five steps (Fig. 6). First, the context is described in order to define protection methods. This initial step consists of five main elements, including the genetic construction (and expected phenotypic changes), the biology of the species, and the country's legislation. In the second step, a list of hazards is drawn up based on the experience with transgenic crops or the fears of the public. The third step involves eliminating the fears that have no associated feasible pathway to harm. In the fourth step, all remaining hazards are classified based on the probability of each pathway to harm and the scale of the expected ultimate damage. Lastly, the fifth step involves making a decision regarding the acceptability of the risks detected.

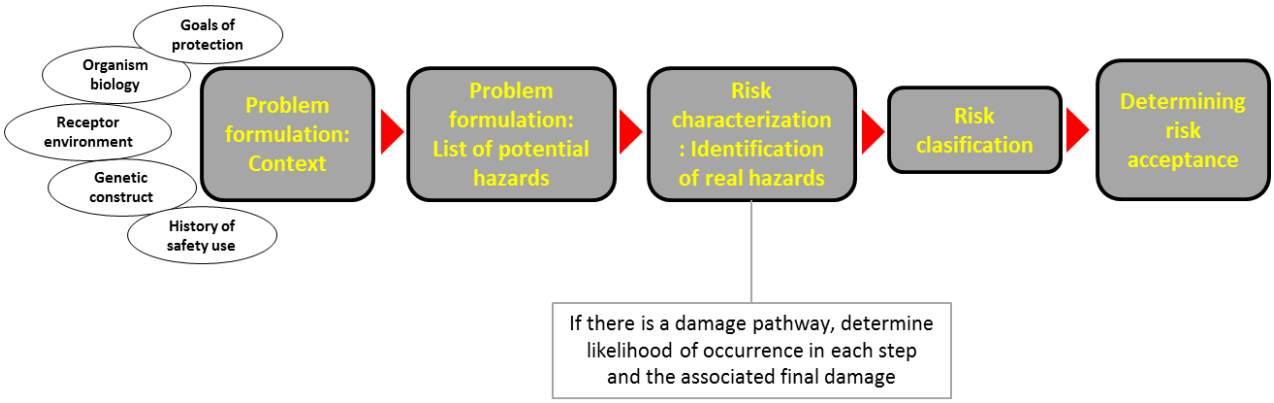

Figure 6. The five steps of risk assessment.

Once the risk assessor has gathered sufficient data about the genetic construction and its expression, the biology of the organism and the changes caused by transgenesis, the receptor medium of the GMOs and information about the safe use of GMOs or plants with similar genetic traits, specific protection targets can be established in line with the country's broader legal framework.

The process step by step

Let us take a specific tree species –eucalyptus– as an example, since it is impossible and even counterproductive to generalize. In Costa Rica, the tree grows in areas with average rainfall of between 100 and 1800 mm/year. Eucalyptus is an exotic species without wild relatives that takes many years to flower. Propagation is achieved using commercially produced cuttings or micropropagation techniques, and the tree is not used in the production of foodstuffs for human or animal consumption (except for some types of honey). Based on the biology of the species, therefore, what protection objectives can be envisioned?

The protection objectives or goals should be directly related to the context (Fig. 6, above) regardless of the potential hazards we may envision (third stage of the risk assessment). The

legislation is designed to protect biodiversity, water and soil quality, iconic species and achieve other, very general objectives. The risk assessor must select the assessment endpoints, represented by species and/or environmental characteristics that can be measured and adequately reflect the broader protection objectives.

Obviously, the assessment endpoints must also be closely related to the context. The following are usually included as assessment endpoints:

- Insects that are beneficial for agriculture.
- Emblematic or iconic species that may be present in areas where GMOs are planted.
- Species of special ecological interest that may be present in areas where GMOs are planted.
- Certain soil and water invertebrates that are used as quality indicators.
- Chemical and physical composition of the soil.

Of course, an assessment endpoint only needs to be considered or investigated if it meets the following two conditions:

- During step two of the risk assessment, hazards to the protection objective are identified.
- In step three, a feasible pathway is identified that links the GMOs to harm at the assessment endpoint.

It is pointless to perform experiments in the field if there is no assumption of causality or if the chosen assessment endpoint does not adequately represent the protection objective.

After determining the endpoints for the assessment of the protection objectives, the assessor proceeds to stage two of the problem formulation process: the drawing up of a list of hazards, which are not necessarily based on a scientific assessment. This step should include any hazards perceived by the different stakeholders.

The main hazards attributed to biotechnology of forest species are, essentially, the same as those already identified (but not found) for the transgenic crops currently available in the marketplace. The following is a list of the principal hazards:

a) The flow of genes to native species (for all events)
b) GM eucalyptus gene flow for commercial and non-commercial conventional eucalyptus
c) Impact on non-target insects (for constructions that express insecticide and RNAi proteins)
d) Impact on flora and fauna in general (for all events)
e) Impact on soil and water (for all events)
f) Propensity to become a weed (for all events)
g) Competition with native species (for all events)

The aforementioned hazards (and many others cited frequently on websites that oppose biotechnology) are generally reinforced by the fact that tree species live longer than grains. However, this factor does not apply in a risk assessment, since each case is analyzed separately

The list of hazards would be considerably longer if each individual´s perception of risk were to be taken into account. However, in the case of field assessments it is essential to establish a

pathway to harm for each hazard, in which the last stage is the impact at the assessment endpoint (or parameter).

The pathway to harm is the core element of the *risk characterization* (step three) and is based on information drawn from laboratory experiments, greenhouse studies and, if necessary, field assessments. It is necessary to establish a pathway involving various steps (or hypotheses) for each hazard, carefully calculating the probability of occurrence. If there is a probability other than zero for all the hypotheses, the final probability is the product of all of the aforementioned probabilities. The magnitude of the harm associated with the pathway should also be estimated. In the case of eucalyptus, gene flow to native species is non-existent, since no native species are sexually compatible with commercial GM species. Therefore, any pathway to harm is immediately ruled out, since this is the first stage (or hypothesis) of any pathway. Consequently, notwithstanding the genetic event, GM eucalyptus cannot transfer genes to the native species of Costa Rica (or of any other Latin American country).

The second hazard (b) must lead, like all other hazards, to harm to the protection objective (or goal). Therefore, one or more of the assessment endpoints must be affected by a conventional eucalyptus tree that has received transgenes from a GM variety of eucalyptus. It is not valid to argue that the gene flow could impact the non-transgenic eucalyptus market, because economic factors are not considered (it is a specific question of coexistence), nor are they represented by any of the assessment endpoints in any sensible risk assessment. If massive transgene flow towards conventional eucalyptus occurs, all the possible hazards listed from c to g could occur with these naturally "transformed" plants. Therefore, it would be important to assess the likelihood of significant gene flow after the normal handling of eucalyptus. An incomplete pathway to harm (with no impact on a specific protection object) could be devised just to assess this condition (Fig. 7).

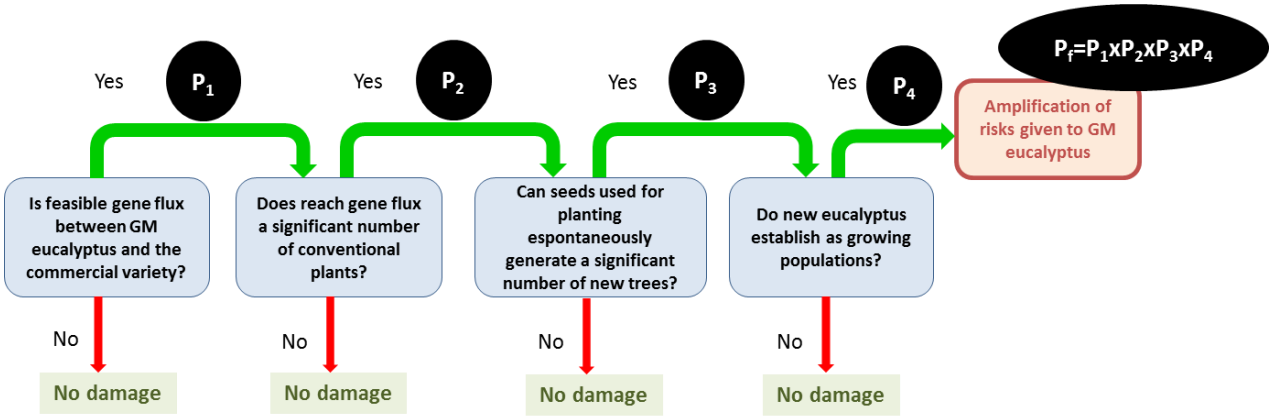

Figure 7. Partial pathway to harm showing the steps (hypotheses) leading from the flow of genes to the amplification of the risks associated with the increase in the population of eucalyptus trees that received transgenes. The probability of each hypothesis being true is shown as P and the final probability is the product of the four probabilities.

If the first hypothesis is correct, the flow of genes is possible among eucalyptus species brought to the Americas. Thus, P_1 may be assumed to be 100% (in other words, $P_1 = 1$). In the second case, it must be borne in mind that transgenic eucalyptus may be planted for commercial

purposes near conventional eucalyptus. Account must also be taken of the fact that the rules governing coexistence are generally established by regulatory and oversight bodies. In this case, one can foresee that crossbreeding between GM and conventional plants is greatly reduced. Therefore, it is fair to assume that P_2 is very small. The situation referred to in step three can largely be discounted as well, since the seeds are not used to plant eucalyptus for commercial purposes, and there were no reports of the germination and establishment of spontaneous eucalyptus populations in the Americas. Therefore, P_3 is also very unlikely. Finally, the situation in step four can also be discounted, since the soil conditions in Costa Rica do not permit spontaneous colonization by commercial varieties of eucalyptus (*E. grandis* and *E. urophylla*). Once again, the possibility is very small (P4). Thus, the four probabilities taken together give only a negligible probability.

The flow of genes may result in large populations of transgenic plants only if the transgenes endow the plants with a great capacity to compete and a tendency to become invasive. Many genes often need to be modified to change a plant´s behavior, however, so no single new trait, or even half a dozen of them, will make eucalyptus an invasive species.

The same approach used to assess topic (b) can be adopted to evaluate the remaining aspects. In short, the main concerns are as follows:

- Impact on non-targeted insects: A pathway to harm may be established efficiently in laboratory experiments. The impact on non-targeted insects has been found to be nonexistent for all the transgenic plants studied hitherto, and the same is likely to be true of eucalyptus if the same genes are used.

- General impact on biota: In addition to being insect resistant, as discussed previously, the objective of genetic changes in forest species is to create tolerance to herbicides and modify the lignin content and other traits. None of these represents an evident pathway to harm. Since assessments are always undertaken on a case-by-case basis, it is necessary to establish a pathway to harm for the new traits expressed in GM eucalyptus. As already noted, the information is obtained from laboratory experiments and greenhouse studies and, if necessary, field assessments.

- Impact on soil and water: GM eucalyptus cannot differentially modify water and soil quality. With hindsight, the soils used to grow transgenic crops have not shown any significant changes, and the few slight changes that did occur were reverted quickly through crop rotation. It is evident that in the case of commercial forests the presence of a transgenic variety for a period of many years can pose a problem. However, pathways to harm can only be established on a case-by-case basis and generalizations should not be allowed.

- Invasiveness and “weeds”: These two dangers are paradigmatic and redundant elements of all risk assessments. Essentially, they are imaginary hazards for plants that have been domesticated by human beings. Most forest species, however, have not been domesticated. Therefore, some may behave like weeds under different circumstances. Only in the case of the latter may it be important to determine whether genetic modification has led to greater invasiveness. This does not apply to GM commercial eucalyptus species (*Eucalyptus grandis, Eucalyptus urophylla* and their hybrids, Gordon et al. 2012).

To conclude, the impact on the environment of the introduction of a GM variety of eucalyptus in Costa Rica will probably be negligible. However, the need for painstaking studies may be

inevitable due to the lack of a preliminary risk communication, field tests and the analysis of a request for commercial release. Even in those cases in which authorization to market a variety is obtained reasonably quickly, the lack of an effective risk communication program will lead to the imposition of disproportionally complex risk management, due to public pressure.

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2.3. Regulatory processes for a genetically modified pineapple as a guideline for risk assessment

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Genetically modified (GM) crops have been used in agriculture since 1996. Today, more than 90% of the soybean, maize, cotton, sugar beet and canola grown in the US are GM. GM crops including Hawaiian papaya, squash (zucchini), sweet corn, sweet peppers, tomatoes and rice have been grown for food consumption. More than 80% of Hawaiian papaya imported to the USA is GM.

Conventional breeding in pineapple is difficult due self-incompatibility, heterozygosity, low diversity, and long generation (seed-to-seed) time. Also, it is impossible to breed for traits such as new flesh color or flowering control in pineapple. In this work, genetic engineering has been used to produce pineapples with pink/red flesh color and flowering control trait.

The objectives were:

1. To produce a unique and differentiated variety of pineapple by accumulation of high levels of carotenoids, in particular lycopene that produces red internal color while retaining most of the characteristics of the parental line, MD2 (Del Monte Gold Extra Sweet Pineapple). The red color will allow consumers to distinguish between GM and non-GM pineapples and it confers nutritional benefits.

2. To achieve the controlled flowering trait by altering expression of genes involved in ethylene biosynthesis in the meristem. This trait allows more reliable programmed production, as well as improving the quality of pineapple and reducing the costs of production (lower harvesting costs, less pesticide use).

To increase accumulation of lycopene in edible tissues of pineapple fruit, we have used phytoene synthase (PSY) gene from tangerine under transcriptional control of the promoter of the pineapple bromelain inhibitor, a fruit specific gene, to increase lycopene in the flesh. We have also suppressed lycopene β-cyclase and/or lycopene ε-cyclase gene expression using RNA interference (RNAi) technology.

In pineapple, ethylene promotes flowering. To achieve flowering control trait in pineapple, we isolated a meristem-specific ACC synthase gene and constructed in such a way to suppress the production of endogenous ACC synthase in the meristem using the RNAi technology. All of the genes above are from pineapple except PSY, which is from tangerine. SurB-Hra gene from tobacco was used for selection in tissue culture, which confers resistance to chlorsulfuron herbicide.

We used *Agrobacterium tumefaciens* to transform MD2 in tissue culture and produced 623 transgenic lines (23,517 plants) in our laboratory in Richmond, California. Transgenic plants were shipped during 2008 to Costa Rica for field trials and testing. Plants were grown in the greenhouse for 15-20 weeks, then in the field according to MD2 production practices, with the exception of plant density. Plants were grown in one row per bed, instead of two, to allow technicians to get into the field easily to collect data. After 16-18 months in the field, plants were forced (by application of ethylene) to produce flowers. Fruits were harvested and cut to assess internal flesh color and quality characteristics (Brix, citric acid, ascorbic acid and pH). Only plants that had fruits with internal red/pink color and acceptable internal quality were advanced for further propagation in the field or in tissue culture. Eleven lines were selected and propagated in the greenhouse and in the field and later line EF2-114 was selected as a lead event.

EF2-114 was established in tissue culture by culture of crown meristems. Six months later, large-scale production started using bioreactor methods of propagation. The propagules were grown in the greenhouse and then in the field for evaluation. Randomized block design with three replicates (each with 200 plants) was used. Plants were randomly selected for data collection for plant and fruit traits.

Both EF2-114 and MD2 fruits were grown and harvested using standard practices. Fruits were used for nutritional analyses, quality traits and gene expression analyses. Fruits were shipped to the US for compositional analyses by ABC Research Company. Gene expression analyses were done in our laboratory in Richmond, CA and Syd Labs, Inc. in Malden, Massachusetts.

Nutritional analyses show that EF2-114 and MD2 are similar for nutrition composition (showing no statistically significant differences) with the exception of lycopene and beta carotene. Agronomic performance analyses including growth rate, plant and fruit traits generally show no difference between EF2-114 and MD2. EF2-114 also is comparable to MD2 for fruit internal quality traits. We are currently studying EF2-114 fruit to define its ripening parameters, quality attributes (taste, aroma,), etc.

Leaf samples were collected from field or tissue culture for molecular analyses to show the presence of genes in EF2-114, T-DNA integration patterns and stability during field or tissue culture propagation. Results indicate that there are two copies of carotenoid genes and one copy of flowering control gene in EF2-114. There are no bacterial genes (including plasmid backbone) inserted in this event. The stability of the genes has been confirmed in tissue culture propagation and over three generations of field propagation.

Studies that indicate that GM pineapple has no adverse effect are summarized below:

- Safe products: expression of genes derived from edible plant species does not produce unsafe products (Hirschberg, 2001; Fraser and Bramley, 2004; Shewmaker *et al*., 1999).

- Very limited seed dispersal. Seed will remain contained in the fruit because commercial pineapples have no seed releasing mechanism (Del Monte data). In addition, the seed is not used for commercial planting. Seed germination and establishments of seedlings in nature is a very rare event.

- Cross pollination is limited with distant varieties: Collins (1960) observed that even when compatible cultivars were planted in adjacent rows, pollination did not occur.

- Possibilities of gene flow to other bromeliads: within a radius of 1 km of the trials, there are no native plant populations or *Ananas ananassoides* and other native species. Spontaneous creation of hybrids is almost impossible (Del Monte data).

Data collection for regulatory process in the US and Costa Rica is in progress. USDA has already made a decision that EF2-114 does not require a movement permit for importation into the USA subject to FDA approval. The data package to be submitted to FDA includes the following topics:

- Transformation method
- Molecular characterization of introduced DNA
- Transgene Copy Number
- Characterization of T-DNA Inserts
- T-DNA insert junction analysis
- Analysis of presence of plasmid backbone DNA from outside the T-DNA region
- Suppression or overexpression of RNA for the introduced genes
- Inheritance and stability analyses
- Nutritional composition analysis
- Food safety assessment
- Post-transcriptional glycosylation of over-expressed gene products*
- Toxicology and allergenicity of over-expressed gene products*

*For the last two topics, bioinformatics analysis of SurB-Hra and Psy proteins of EF2-114 was done to assess potential allergenic cross reactivity to known and putative allergens. Analyses found no concern in this regard.

In Costa Rica, we have worked with the MAG/Biotech Commission for the field trials since December 2005 and have implemented all governments regulations needed. We have also reported to MAG on our operation and handling of the materials regularly via an auditing third party company. In addition, we have obtained permit from MAG to grow up to 200 ha EF2-114.

To obtain Costa Rica approval for EF2-114 commercial production and export, we propose to present the following:

1. Environmental package including USDA decision and studies or literature on “No impact on environment.”
2. Food safety package.
3. Strategies and characteristics to prevent mixing of GM and non GM pineapple
4. Our field studies on agronomic performance, fruit traits and internal quality analyses, and plant traits analyses comparing EF2 and MD2.

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2.4. Discussion panel on basis of risk assessment, applications in agriculture and forestry

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Panelists: Phil Macdonald (Canada), Marianela Araya (UNEP-GEF), María Mercedes Roca (Zamorano), Paulo Paes (Brazil), Ebrahim Firoozabady (USA)
Moderator: Pedro Rocha (IICA)

The participants wrote down and read out their questions to all the panelists. The questions were grouped together by topic. Each panelist was given the opportunity to respond to each group of questions. The following section summarizes the discussion that ensued.

2.4.1. GM Pineapple

MD2 is the traditional variety of pineapple that accounts for 90% of all exports worldwide. EF2 is the GM variety. Development of GM pineapple got under way in 2002, and it took the researchers involved eleven years to achieve the genetic transformation of the fruit. Using the transformation method available at the time, the process would have taken six years. However, since it would have cost USD2 million to use that method, the company decided to start from scratch and develop its own method of genetic transformation.

At that time no one had identified or isolated a gene that could be inserted into pineapple, so the process took longer because a gene and the promoters had to be identified. Given the major investment in time and money that was required, the company decided to patent the promoters, the transformation process, etc.

The genes that were inserted into GM pineapple include one from tangerine and two from pineapple. All the additional DNA elements, promoters and terminators, came from pineapple. A tobacco gene was also used, though only for the selection process. Pathogen resistant genes were not inserted into this GM pineapple. The company is currently developing projects involving pathogen resistant pineapple (in Brazil and Costa Rica) which are separate from the GM pineapple project described. For now, they expect to generate disease-free materials through in vitro tissue culture.

Some 70% of the GM pineapples produced are expected to be exported to other markets. The remaining GM pineapple will be used in the Costa Rican market, as fresh fruit or for processing. The company is currently obtaining the permits for consumer testing.

2.4.2. GM maize in Honduras

Although GM technology for maize has been adopted by small farmers in Honduras, large companies account for most of the acreage of GM maize. According to official statistics, the country 35,000 hectares planted with GM maize. Structural and social constraints in the developing countries make it difficult for smallholders to invest in GM technology, mainly due to

the high cost of seeds. While the economic benefits are evident once the harvest is in, initial investments or loans are not always an option for small farmers.

Honduras uses GM maize for its school meals program. Children consume it in tortillas that have lower levels of mycotoxins.

2.4.3. Risk communication

Ever since the commercial release of the first GM crops was authorized, breeders have been reactive rather than proactive with regard to communication activities. The release, marketing and adoption of GM crops should have been complemented with effective education and communication strategies. Scientists focus on research and GMOs are developed in the laboratory. In most cases, communication has been neglected, clearly affecting the user of the technology and the end consumer.

By contrast, opponents of GM technology (or "transnational activists") have focused their efforts on communication campaigns that offer information that is often biased, inaccurate or false, based on assumptions rather than facts. Moreover, these groups are organized, have a common goal and receive funding. A common tactic of the opponents of the technology is to question and disparage rigorous scientific results, offering instead mere unfounded assumptions. They also claim the high ground by mixing technical, economic, social, philosophical and other arguments, which only creates confusion.

Canada's risk assessment process includes a risk communication component whereby all stakeholders are consulted. All applications for approval of GMOs are public documents (the information is available on line, although some information is confidential). The public is able to submit comments within a specific timeframe. The country´s regulatory agency is required to respond to all comments or questions. Details of the site used for field trials, for example, are kept confidential, to prevent the crops from being vandalized.

As part of the communication process the Canadian government holds activities in schools and with different target groups. Ironically, these activities have been heavily criticized and, as a result, are now carried out less frequently.

2.4.4. Impact of the adoption of GMOs

The potential benefits of GM maize for consumers include the fact that the grain is of a higher quality because it contains lower levels of pesticides and mycotoxins. The number of pesticides and the frequency with they are applied are greatly reduced. The absence of mycotoxins is an indirect result. The presence of fewer insects means that the grain suffers less physical damage. That, in turn, limits the capacity of fungi to colonize the substrate and so prevents the production of mycotoxins, which cause health problems that can be fatal.

A participant asked whether Canada had documented harm from GMO use in the past 20 years. The answer to that question was that no such harm had been reported. In fact, the expert was able to cite the following three documents published by Canada on: 1) the economic benefits of the adoption of herbicide tolerant canola; 2) the environmental benefits of the adoption of herbicide tolerant canola; and 3) the reduced use of pesticides/herbicides as a result of the use of biotechnology. A clear example of the benefits for Canadian farmers was the fact that GM-Bt maize had the effect of controlling the European corn borer pest.

2.4.5. Background information on risk assessment

The agronomic and productive performance of a GM crop must be assessed in the field. For example, in Canada the evaluation of agronomic aspects is very important, because the latter are considered part of the country´s sustainability goals. In some countries, however, such assessments do not form part of crop biosafety and, consequently, are not subject to risk analysis or under the responsibility of a biosafety committee. Some companies ask research centers or universities to perform growth or pest control assessments to ensure the quality of the materials they sell.

The experiments that substantiate the data used in risk assessment activities must be performed by the company that developed the GMO for potential commercialization. Firms seeking a permit to release GMOs in a given country must cover the cost of the risk assessments and guarantee the quality and safety of their products. Country regulators must be trained to handle applications for the commercial release of GMO crops and possess the expertise required to evaluate dossiers and provide the necessary follow-up.

For dossier analysis, the competent national authority may draw on existing information or assessments carried out in other countries. This is known as data transportability and familiarity, i.e., information related to a particular GMO already exists in another place (country) and other countries may refer to it in reviewing dossiers.

Canada's situation differs from that of many countries. In Canada, risk assessments are performed by the public sector, by government regulators. The applicant must submit all pertinent information for the regulators to conduct the risk assessment. Public and private risk assessments are both valid, however. Each country decides which option to use, and its decision may be influenced by the resources available.

The process of applying for permission to release a GMO varies from country to country. However, the common denominator is that it is a long and tedious process, which seems to preclude the possibility of research centers, universities and small companies from obtaining permits. The process of obtaining approval to plant GM crops is so difficult that normally only large companies have the time and resources to undertake it.

A successful case of a state-owned enterprise that developed technology and subsequently obtained approval for a GM crop (bean 3.1) is Embrapa (Brazil).

A general protection objective may be the protection of biodiversity, particularly in the case of countries that have signed the Convention on Biological Diversity. Such a protection objective is not very useful, however; a more specific objective is preferable, such as the protection of an endangered species like the monarch butterfly. In the case of GM technology, the values of society may also be considered protection objectives.

Data related to molecular characterization may be useful for the approval application process, since it addresses many questions related to phenotype. If applications are submitted without molecular data, phenotypic characterization must be exhaustive.

Canada does not regulate GMOs but rather crops with new traits that may or may not originate from genetic transformation. They may have been obtained by means of radiation, for example. In Canada, risk assessment sets out to answer five questions: 1) What is the trait? 2) What is the proposed phenotype? 3) How will it be used? 4) Will it be used for animal feed? 5) Will it be used for human consumption?

The question was raised of social pressure to perform monitoring activities even though a risk assessment has already been conducted. Such a request is contradictory, particularly if the risk assessment has established that the risks are negligible/irrelevant. Monitoring would not be justified. A key monitoring issue is cost, especially when large acreages of maize are involved. Therefore, GM monitoring should take into account the capabilities of the regulatory agencies or biosafety auditors.

Two types of monitoring measures used in Canada were mentioned. Firstly, measures for insect resistant crops (seed companies are audited to ensure they comply with statutory requirements governing the activity). Secondly, measures that apply to herbicide tolerant crops (monitoring of any real or potential weed resistance). The latter are agronomic measures but form part of the risk assessment process.

2.4.6. UNEP-GEF

With regards to the UNIDO master's degree program in biosafety and the UNDP-GEF perspective, it was emphasized that UNEP-GEF must maintain a neutral stance since it is an international organization and cannot take sides either for or against the adoption of GM technologies.

UNIDO and UNEP-GEF are both part of the United Nations system, although each acts independently. UNIDO's MSc program in Biosafety, for example, is not always used as a training program in countries that execute a UNEP-GEF project, since each country has the sovereign right to decide how to conduct their own capacity-building program. Although UNEP-GEF advises member countries about courses, institutions and training programs available, but it is up to each country to decide whether to incorporate them into projects.

2.5. Closing comments

The following questions must be answered during the problem formulation step of a risk analysis: "What do we want to protect?" "What should be protected?" and "What needs to be protected?"

The need to consider the question of language, the use of terms in different languages, was discussed. Terms such as hazard, risk, harm, assessment, precision, accuracy, possibility and probability do not necessarily have an exact equivalent in other languages, which can lead to misunderstandings or misconceptions.

To wind up the workshop, some of the participants were asked to explain the procedures used to perform risk assessments in their respective countries. The following is a summary of their remarks:

Cuba: In Cuba, pest resistant BT maize is grown commercially. The event was developed by the Center for Genetic Engineering and Biotechnology. Cuba's state-funded National Biosafety Center, established in 1998, is responsible for conducting risk assessments. Assessments are conducted on a case-by-case and step-by-step basis. While the center bases its decisions on technical and scientific elements, social, political, cultural and economic considerations are also taken into account.

Cuba has regulations on biosafety. Resolution 180 establishes all the requirements with which applicants must comply. The process involved is as follows: Once a GMO application is submitted, the dossier is reviewed by a multidisciplinary group of experts (from various national institutions) that makes the final decision.

Bolivia: Bolivia's new regulatory framework (*Ley Marco Madre Tierra y Desarrollo Integral para Vivir Bien - Ley 300*) restricts GM crops and recommends that the presence of GMOs gradually be reduced. Since Bolivia does not have an up-to-date set of biosafety regulations, there are no protocols establishing how GM crops are to be reduced in the country. The question of risk assessment is not addressed clearly and pragmatically in the current regulations (D.S. 24676). Bolivia approved the introduction of GM soybean in 2005, since the crop had already entered the country and the regulations in effect at the time could not be applied properly. The country's National Institute of Agricultural and Forestry Innovation (INIAF) reports that 98% of the country's soybean crops is genetically modified. Monitoring activities conducted in 2010 and 2011 detected unauthorized GM maize and GM cotton. Therefore, Bolivia needs to look at the question of a national biosafety framework again, establish a National Biosafety Commission and train its members, and modify existing legislation taking into account the actual situation and real needs of the country.

Ecuador: Article 401 of Ecuador´s constitution, approved in 2008, states that Ecuador is free from GM seeds and crops. The article also mentions that if the country needs to import a GMO it may do so after a series of consultations. After a lot of hard work, several ministries–including the Ministry of the Environment–progress has been made with planning issues. Biosafety policies have also been established in the National Plan for Wellbeing (2013-2017), as well as a five-year training plan (2013-2018). There is a plan to strengthen government laboratories to meet the needs of GMO risk assessments. Workshops to discuss biotechnology issues have been organized throughout the country, and President Correa studied the information and has agreed to review various articles of the constitution, including Article 401.

Peru: Peru spent several years working with countries with a great deal of experience in the field of biotechnology (Argentina, Brazil and Mexico) on a three-phase risk assessment program for GM crops (pilot, pre-commercial and commercial). However, the country declared a 10-year moratorium on GM crops beginning in October 2011. The regulations governing the moratorium came into force in November 2012. As a result, applications are difficult to process parallel to the moratorium: a global survey of crop baselines was requested and even baselines of soil microorganisms present in Peru's soils. A zero tolerance level has been requested for GMO traces in conventional seed imports (with fines of up to USD8 million for if tests of reactive strips are positive). Many companies have stopped importing maize and soybean, thereby endangering supplies. The establishment of a committee to issue guidelines on the moratorium itself has been requested.

Costa Rica: There is a National Technical Commission on Biosafety comprised of an intersectoral group (ministries of agriculture, environment, science and technology, two NGOs and academia) whose remit is GMOs for use in agriculture. The Commission has operated for more than 20 years and has approved events for several crops, including maize, soybean, new coco yam, banana, plantain and cotton.

Nicaragua: The country has been working on biosafety since 2005, when a ministerial resolution and a presidential decree were issued. That same year, GM maize was approved for use by the poultry industry, leading to the development of certain technical capacities in risk assessment. In 2010, Nicaragua adopted Resolution 7005, which deals with biosafety issues, but there are still no regulations. A Biosafety Committee was established, comprised of representatives of the public and private sectors, academia and environmentalists. The country is currently conducting an assessment of its own capabilities (laboratories, scientists with graduate degrees) with a view to developing a national biotechnology plan that would address biosafety issues.

Section 3: Risk Assessment and Low Level Presence

3.1. Towards a global policy on low level presence[5]

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Low level presence (LLP) is the involuntary presence of low levels of genetically modified (GM) crops in food imported for human or animal consumption when the GM crop is authorized for use in foodstuffs in one or more countries but not in Canada. LLP refers only to material that has been authorized for commercial distribution and, therefore, excludes adventitious presence, which is defined as the unintended presence of pre-commercial or otherwise unauthorized material that has not been assessed for food or feed use and unconfined environmental release in any country.

Due to a significant increase in the number of genetically modified products on the international market, it is becoming increasingly difficult to avoid LLP in loose GM grain in bulk and its byproducts. In addition to the increase in the number of countries that permit GM crops and in the acreage planted, other factors also influence the potential impact of LLP across the globe, particularly the emergence of developers of non-traditional GM crops, an increase in the sensitivity of GM crop detection tests, and isolated and asynchronous approvals of GM crops in different countries.

A study analyzing the possible economic impact of LLP in the Americas, based on the spatial equilibrium model, was recently discussed by the International Food and Agricultural Trade Policy Council. In this study, Kalaitzandonakes and his collaborators present various economic impact scenarios that could occur if obstacles to bilateral trade between certain countries oblige both importers and exporters of grains to find alternate routes for their products. Countries that import large amounts of grains and are dependent on bigger suppliers may be faced with a steep increase in the price of these products (of around 9%-20%). The authors of this study recommend that countries in the region optimize their regulatory capacity to streamline the assessment of the safety of new products available on the market and thus avoid asynchronous approvals. For this reason, they suggest promoting regional collaboration to bolster regulatory capacity, particularly in countries with fewer resources. They also suggest avoiding the implementation of zero tolerance policies towards LLP, which could lead to dramatic increases in food prices and undermine the region's food security.

Mindful of the potential impact of LLP on the global economy and trade, Canada encourages other countries to adopt pragmatic policies for the domestic management of LLP and global solutions for international LLP management. The presence in imports of GM products not approved in Canada, including LLP, constitutes a breach of the current regulations, so the expectation is that there will be a return to observance of the existing rules. The Canadian Food Inspection Agency (CFIA) and Canada's Ministry of Health (HC) will assess each case of non-compliance to determine the appropriate level of intervention required to ensure the observance of the current regulations. The alternatives would be to obtain authorization of the product or to withdraw it from the Canadian market.

[5] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/06%202013-02-27%20LBarnola.pdf

No incidents involving Low Level Presence have been reported in Canada, but in 2010 the AAFC and the CFIA began to review Canada's national policy on LLP management. The main objective of the review is to make the current regulatory system more effective, and to continue to protect food and feed safety and the environment without hindering innovation and trade unnecessarily. Equally important is Canada's effort to provide a model LLP management policy that could be adopted globally. The organizations involved in this effort include AAFC, the CFIA, HC, the Canadian Grain Commission, Environment Canada and Foreign Affairs, Trade and Development Canada.

The proposed LLP policy for Canada that is still under consideration seeks to establish bureaus for handling LLP events, clarifying the focus of risk management and stipulating the conditions under which the implementation regulations would apply to imported food and feed. The specific objectives of the policy include: (a) protecting the health and safety of human beings, animals and the environment while simultaneously minimizing trade obstacles; (b) facilitating an effective and efficient risk-based approach to LLP management; and, (c) providing transparency and predictability for merchants.

The scope of the proposed LLP management policy in Canada applies to grains and their byproducts used for food and feed that contain LLP, provided they meet the two following conditions: (1) the GM crop must be approved by a minimum of one country based on the Codex plant guidelines; and (2) Canada must already have determined that the food safety assessment conducted in the country concerned complies with the Codex plant guidelines. The proposed policy does not apply to seeds for planting, which is being addressed simultaneously at both the domestic and international levels with support from various countries and institutions. Canada's reasons for not including seeds within the scope of this policy include: (a) the absence of international guidelines for assessing environmental LLP risk in seeds; (b) the fact that seeds may replicate freely in the environment; and (c) the possibility that Canadian environmental conditions were not considered during external assessments to determine the relative risk of releasing them into the environment.

The proposed framework for the Canadian LLP risk management policy for grains is based on the following levels:

(1) The level of action (a value, yet to be determined, of between 0.1% and 0.2%) refers to an LLP level above which action will be taken to determine whether the threshold applies or a conformity measure is required. This means that if the LLP detected is below the level of action, no conformity measure will be adopted.

(2) The threshold level is the maximum LLP level up to which no conformity measure will be adopted, provided that Canada has conducted a GM crop risk assessment and found that that the low level presence (LLP) does not represent a risk to human and animal health or the environment, because the concentration does not exceed the threshold level. Unlike a safety assessment, an LLP risk assessment does not influence the decision to authorize a GM product but merely determines the risk level associated with the situation of non-conformity.

If levels (1) and (2) are exceeded, or if it has been determined that a GM crop represents a risk, the proposed policy would not be applicable. A case-by-case analysis would be conducted to determine the response level required to ensure that the product conforms to the regulations.

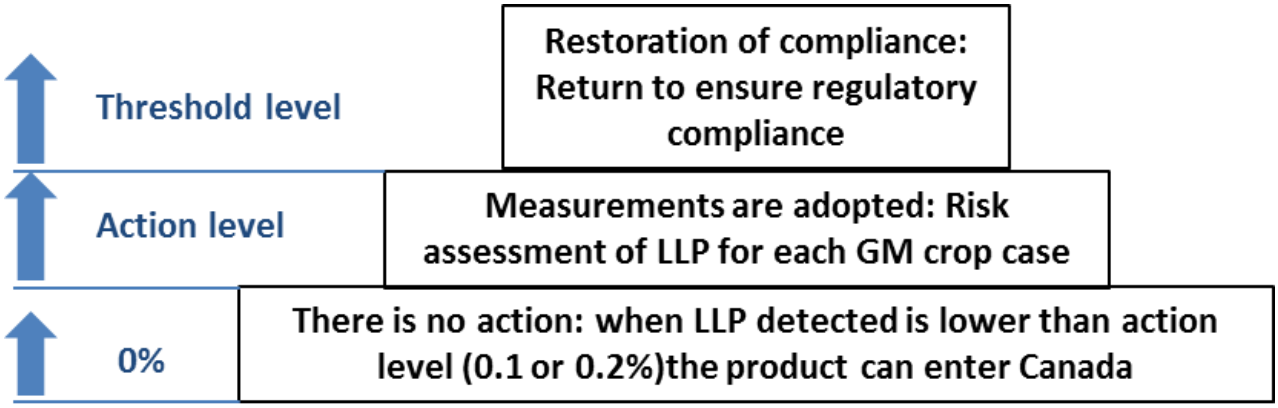

Figure 8. Threshold levels and actions.

To implement the proposed policy, the control and monitoring activities to ensure that the requirements are met will adopt a risk-based approach. Considering that LLP is a minimum source of risk, imported grains will not be subject to frequent monitoring. In addition, monitoring and control of imported grains will take place at entry points and before the grains arrive at Canada's borders.

If an imported grain meets LLP management requirements for the policy proposed by Canada, no response measures will be adopted to ensure compliance with the policy. On the contrary, if an imported grain does not meet the LLP requirements proposed by Canada, a case-by-case analysis must be carried out to determine the level of response needed to make the grain conform to the regulations. The importer will be informed of the requirements, including the authorization process, and notified of the measure(s) needed to comply with the regulations.

On November 6, 2012, Canada implemented a national online consultation to obtain comments from key industry stakeholders and the public at large. The comment period lasted 75 days and all relevant information, including the proposed LLP management policy, its implementation framework, background information, and a list of frequently asked questions, are available online in English and French. In addition, face-to-face meetings were organized with diverse groups, including groups interested in grains, food processing and organic products industries as well as a multi-sectoral meeting. The notification process of the World Trade Organization (WTO) was used simultaneously to inform Canada's international trading partners of the proposed policy for domestic LLP management. The comments received will influence the development of an LLP policy and the final framework for implementation.

Parallel to its domestic work, Canada has been spearheading an international effort to gradually supply information about the possible effects of LLP on international trade, to encourage other countries to promote the adoption of pragmatic policies for LLP management, and the development of international solutions for global LLP management. To that end, Canada formalized the Global LLP Initiative (GLI) in March 2012 during the International Meeting on Low Level Presence held in Vancouver Canada. At that meeting, the participating countries approved the International Statement on LLP and agreed on an international workplan that includes five key activities. In September 2012, the GLI met in Rosario, Argentina, where participating countries reviewed the progress made with the original work plan and agreed to make the International Statement on LLP public. Canada also acted at the bilateral, regional and

international levels and sent high-level officials on missions to key countries as well as to regional and international forums, such as APEC, IICA, NABI and FAO, to address the issue of LLP.

3.2. Low level presence of GMO in agrifood products – Perspective of an exporter country[6]

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Context

The concept of LLP refers to a range of scenarios that will almost inevitably occur, even though mitigation actions are taken to reduce the possibilities. Although such mitigation plans are worthwhile, it is also necessary to prepare plans to deal with the occurrence of low level presence (also known as adventitious presence) of GMOs on a ship, including the measures to be implemented. A real system for addressing such situations needs to be in place, i.e., something more than simply a procedure for rejecting or disposing of the shipment.

Producer countries should not delay approval of this technology until such time as importers do, because importers then take even longer to make a decision. There is a need to implement biotechnology tools in response to the growing demand for food and other agricultural products, the economic and productive development needs of our countries, and the objective of permanently improving the sustainability of agricultural production.

Generally, the origin of low level presence (as mentioned in the Codex Guidelines) is due to:

- Asynchronous approvals of transgenic events by the different countries. The developer/producer countries where GM crops are grown approve an event, which is then cultivated and may appear in low levels in exports to other countries where the event has not yet been assessed. The approval policies of certain countries may directly influence asynchronicity. For example, certain important importers embrace a policy of waiting until the exporter country commercially releases a product in order to assess an event. This means that there will inevitably be asynchronicity.

- Low level presence in seed imports. Occasionally, the importation of non-genetically modified material or material assumed to be non-genetically modified may include certain events approved by the destination country. There may also be a low level presence in seeds with unapproved events in the country importing them. This will eventually lead to LLP in the grain that is grown and exported to that country, which will result in an even more difficult scenario for the final importer than the first.

- Discontinued events: This occurs when an importing country follows a policy of approving events for a limited time. A flow of imports begins in which the presence of an event is acceptable, but years later the developer of the event is no longer interested in renewing the approval, and the authorization expires. By contrast, the principal exporting countries approve events indefinitely, taking the view that a limited authorization does not make sense from a scientific or fair trade standpoint. So the event may continue to be present in

[6] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/07%202013-02-27%20LLP%20Lema.pdf

exports for some time even if it is discontinued by the exporting country, especially in the case of autogamous crops.

The situation described above may be combined with the entry into the public domain of the first biotechnology events, following the expiration of their initial patents dating from the 1980s and 1990s. In certain cases, this can lead to less centralized production of seeds, making it more difficult to control it, and the original breeder may lose interest in renewing the permits.

Another important issue related to LLP is the impossibility of achieving 100% segregation for an affordable cost at the national and international levels. The lower the level of tolerance, the more expensive the procedures needed to fulfill the requirement. In this case, all the previous studies carried out on the cost of GMO segregation are valid—for example, those conducted in relation to the phrase *"may contain"* in the Cartagena Protocol.

Bilateral LLP initiatives (a producing country enters into a dialogue with an importing country) have so far produced few effective results. Recently, multilateral initiatives have arisen, particularly given the need for consensus in the face of such a range of criteria and interests with regard to the matter. Such initiatives include:

- The Codex Alimentarius Guideline on LLP for food products. These guidelines have a solid scientific basis and have been the object of much discussion at conferences involving all stakeholders with vested interest in this topic (producers, consumers, developers, NGOs). These guidelines do not propose a universal threshold for LLP assessments but rather a scientific, case-by-case approach.

- The FAO initiative to implement the Codex Alimentarius guidelines. These actions are divided into two groups: 1) within the multilateral group, support for the creation of an expert group by the FAO/Codex to perform non-binding safety assessments that countries can use as a reference when they need to resolve a LLP situation quickly; and 2) implementation of the FAO database on authorizations of safety assessments of different events that have been completed.

- The OECD guideline for LLP (still under negotiation). These guidelines are designed to help countries establish procedures for resolving LLP issues in seeds and in the environment.

- The International Life Sciences Institute (ILSI) initiative aimed at developing LLP guidelines. Non-binding guidelines that would serve as a reference for environmental biosafety assessments for LLP in seeds.

- The Global LLP Initiative. This is an intergovernmental forum that promotes direct interaction among the main producers and importers of GM-based agricultural products in order to promote the national implementation of the standards mentioned in the previous sections. Two meetings were held in 2012, the first in Vancouver, Canada and the second in Rosario, Argentina.

Although progress has been made under multilateral initiatives on LLP, importer countries need to collaborate or be able to understand this issue. Their engagement should occur spontaneously based on their analysis of their own needs and interests, especially in relation to the following topics: **cost** (zero tolerance calls for the investment of resources to ensure that products are free of adventitious presences); **demand** (countries have different LLP criteria, i.e., some accept higher levels of tolerance to GM events, which makes them preferred destinations for such products); and **food security** (zero tolerance reduces the number of countries from which food

can be obtained, starting with the world's biggest suppliers. Supplies then become less homogenous and more unpredictable).

Global LLP Initiative for agrifood products

As previously mentioned, this is a multilateral effort to resolve LLP issues for GMOs proposed and led by Canada. It currently comprises a number of countries: Australia, Argentina, Brazil, Canada, United States, Chile, Costa Rica, the Philippines, Indonesia, Mexico, New Zealand, Russia, South Africa, Uruguay and Vietnam; the European Union and China participate as observers. This group met twice in 2012, in Vancouver, Canada and Rosario, Argentina. Topics currently addressed by the group include: 1) origin and implications of LLP situations that may occur through trade in agricultural products; 2) development of a strategy to focus on LLP at the international level; and 3) drafting of an "International Statement on Low Level Presence" and a Work Plan. The statement, which shows the level of understanding achieved so far by the member countries, is to be found in Annex 2.

3.3. Costa Rica´s experience in LLP as an importer country[7]

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Statement on a global policy on the low level presence of GMOs

- Recognizing the need for action, the representatives of the following governments [Australia, Argentina, Brazil, Canada, Chile, Costa Rica, Germany, Indonesia, Mexico, New Zealand, Paraguay, Philippines, Russia, South Africa, United States, Uruguay and Vietnam]...

- We recognize the importance of developing practical approaches for the management of LLP that are science-based, predictable and transparent, and that will encourage the use of international science-based guidelines on LLP, such as the Codex Alimentarius Annex 3: Food Safety Assessment in Situations of Low-Level Presence of Recombinant-DNA Plant Material in Food.

- We recognize that the approaches could be implemented on a voluntary basis by countries.

Definition of LLP (low level presence)

Unintended presence, at low levels, of genetically modified organisms approved in the country of origin but not yet authorized in the country of import.

Objective of the coalition of member countries on a global policy on the low level presence of GMOs

To work together to address the risk of interruptions in trade due to LLP situations, and facilitate international trade in agricultural products by developing practical methods that include both food and feed.

Workplan of the coalition

- Establish a mechanism to ensure the permanent exchange of information on the countries' experience with LLP management at the national level.

[7] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/08%202013-02-27%20AMay.pdf

- Develop an International Engagement Strategy on LLP.
- Develop a proposed approach, or set of approaches, for global LLP management, including the participation of a multilateral organization.
- Explore practical methods of reducing asynchronicity in submittals, assessments and approvals.

Concept of asynchronous approval

Asynchronous approval refers to a time gap between the regulatory authorizations in the country of origin and country of import. It has the effect of delaying the introduction of new crop technologies and creating the potential for the expensive and wasteful interruption of trade in safe agricultural products.

The following factors contribute to this:

- Different regulatory and legal requirements to assess and approve products derived from agricultural biotechnology.
- Other issues that affect predictability in the countries with regard to the review of regulations.

Practical ways of reducing asynchronicity

1. Encourage submittal of dossiers to regulatory authorities of key export markets and include those events intended for domestic use that may be combined with exported crops
2. Promote the adoption of a standardized dossier, whenever possible
3. Identify and assess the possibility of changing or deleting aspects that are redundant or lack a scientific basis from food and feed safety requirements
4. Facilitate the development of a database for global, Web-based information to update new dossier submittals and approvals.

Participation of an international organization in the issue of LLP

Codex Alimentarius. Joint commission of the FAO and the WHO.
Annex 3 of the *Codex Alimentarius*: Food Safety Assessment in Situations of Low-level Presence (LLP) of Recombinant-DNA Plant Material in Food (*Annex to the Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* [CAC/GL 45-2003]).

Agreements of the first International Meeting on LLP

- Develop a practical approach, or set of approaches, to LLP management that is science-based, predictable and transparent; encourage the use of international guidelines on LLP, such as Annex 3 of the *Codex Alimentarius*.

- Importing and exporting countries will work together to address LLP to facilitate international trade in agricultural products based on the development of a practical approach.

- Define LLP as low levels of recombinant-DNA plant material that has been subject to a safety assessment pursuant to the *Codex* guidelines in one or more country, but which occasionally may be present in foodstuffs in importing countries in which the safety of the recombinant-DNA plants has not been determined.

- The practical approach, or set of approaches, to LLP management should not pose a threat to human and animal health and safety, or to the environment.

3.4. Discussion panel on LLP

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Speakers: Martin Lema (Argentina), Alex May (Costa Rica), Luis Barnola (Canada)
Moderator: Pedro Rocha

3.4.1. Central American Initiative on Biotechnology and Biosafety (ICABB)

The ICABB initiative arose out of a formal request made by the Competent National Authority of each country and is similar to other initiatives in the region, such as the NABI and the Grupo 5-CAS.

The countries in the region requested that IICA provide an opportunity to discuss issues of interest pertaining to biotechnology and biosafety, which led to a needs assessment workshop being held in Panama in 2012. A document was produced at that event and its final version was presented to the CAC ministers of agriculture. ICABB was formally established on February 25, 2013.

The process of creating and setting up the ICABB was quite quick and unhindered by operational or administrative difficulties in organizing the group. Group discussion emphasized policy harmonization, integration of issues and knowledge (LLP, risk assessment, monitoring, introduction of new technologies, coexistence, etc.). In the case of Costa Rica, there is strong political support for its participation.

3.4.2. LLP

Argentina: The country has not established a tolerance threshold for LLP seed and is currently drafting regulations that include an LLP mechanism. The regulation lists the events that are most likely to affect the country. Safety assessments must be executed based on the assumption that levels should not exceed the quality thresholds for "off type" protocols or other varieties.

Argentina has had cases of the presence of seeds with events that have not been approved by the country, such as canola and alfalfa. In one instance, the protocol called for the destruction of the seeds. In the second, the event was detected in crops out in the field that were eventually destroyed. However, the country is looking to move forward and establish a policy framework that considers these types of detections.

Paraguay: The country has already established a threshold for maize and cotton.

Costa Rica: Threshold tolerance (for grains) has not yet been addressed at the national level, but will soon be discussed as a part of a second step. The country has begun to coordinate with seed companies and discuss practical measures in order to avoid any unintended presence of GM seeds and establish seed quality and purity guidelines.

3.4.3. Approval of GMOs in the countries

China: The country's approval of GMOs is unique since it requires that the GMO be approved by the breeder/exporter country before they conduct their own assessment. This regulation is not realistic since there are certain GMOs not currently approved by the breeder country (United States, for example), but which are approved by third world countries (Argentina and Brazil, for example). This will lead to even greater issues of asynchrony during the approval process.

Argentina: Argentina's approval process is different from China's in that, as an importer, it will approve an event if it is already approved by the exporter country.

Costa Rica: A group of experts is currently at work on a scientific and legal mechanism for GMO approval that accepts approvals from the GMO exporter or breeder country.

Another possibility under consideration for GMO approval is for importer countries to develop their own safety assessments, allocate their own resources for that objective and disregard any prior references for the GMO from other countries. This would lead to an inconsistent approval system, however, and the same would be the case if an importer country performs an assessment to approve or reject a GMO and, in addition, also requires the exporter country to do the same, thereby undermining the importer country's GMO assessment system.

3.4.4. Tolerance threshold

At the scientific level, it is difficult to establish the tolerance threshold. Instead, threshold numbers have been established, either randomly or by consensus. With regard to seed types with GM events that are not approved by a country, a practical method is to establish a tolerance threshold. If the GMO event exceeds the threshold level, the shipment is denied entry. A threshold also avoids many economic concerns: a high threshold (5-10%) simplifies the approval procedure for importers. A very low threshold, however (0.1-1%) makes it nearly impossible for the importer country to comply with the level.

International discussions have considered a risk assessment that is based on a threshold identical to quality standards for conventional (non-GM) seeds. The rationale is for every seed to comply with equal levels of quality standards or purity, and equate that of GM seed varieties to non-GM seeds.

3.4.5. Criteria for an LLP risk assessment

Risk assessment guidelines for processed foods are based on Annex 3 of the *Codex Alimentarius,* which covers low level presence in food products. Annex 3 is based on the experience of various countries where GMO presence has not yet been pre-authorized.

However, seed risk assessments have not progressed for various reasons. For example, a biosafety assessment for low level presence should focus on the potential of GM crops to become weeds (invasiveness, persistence). In this case, genetic modification may potentially improve crop performance in this area.

Section 4: Risk Assessment in Genetic Modified Animals

4.1. *AquAdvantage* Salmon – A transgenic Atlantic salmon genetically modified for fast growth [8]

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AquAdvantage Salmon is a transgenic Atlantic salmon that has been genetically modified to grow faster than a conventional (non-genetically modified) Atlantic salmon. It was developed by AquaBounty Technologies (ABT), a US-based public biotech company dedicated to developing high-tech productivity enhancements for the aquaculture industry. Work on AquAdvantage Salmon first began in 1989, when ABT created the first founding stock of transgenic salmon. In 1995, ABT opened a New Animal Drug Application with the U.S. FDA, and in 2001 ABT submitted to the FDA the first of 28 scientific studies comprising the technical dossier of the AquAdvantage Salmon. In 2010, the FDA presented their findings, basically the results of their internal technical review, to an independent technical committee (VMAC) comprised of industry and academic experts, in which they concluded that the AquAdvantage Salmon was safe for human consumption and safe for the environment. The VMAC committee reached a similar conclusion, and so the AquAdvantage Salmon is awaiting final official approval by the FDA. If approved, the AquAdvantage Salmon would be the first genetically modified animal approved for human consumption in the history of the FDA, and of humankind. AquAdvantage Salmon is also the most scientifically studied fish in the history of aquaculture.

The AquAdvantage Salmon was developed by inserting a genetic construct (opAFP-GHc2) comprised of a growth hormone gene from the Chinook salmon and a promoter and terminator sequences from a marine fish, the Ocean Pout (Fig. 8). The genetic construct is fully integrated into the genome of the Atlantic salmon, which ABT successfully demonstrated in heritability and durability studies over eight successive generations (Fig. 9). The AquAdvantage construct allows the Atlantic Salmon to more efficiently utilize its endogenous growth hormone metabolic processes in order to achieve accelerated growth, especially during early phases of the salmon's biological development. The result is a growth rate superior to that normally experienced in non-genetically modified Atlantic salmon (Fig. 10). The benefit to the aquaculturist is obvious—the fish reaches market size in less time than a conventional farmed salmon. The AquAdvantage transgene is only biologically active in salmonid fish, and cannot be transferred in a functional form to other organisms, including microorganisms, from the AquAdvantage Salmon.

[8] This presentation was given by Judith Ivette Vargas. The text was contributed by Henry Clifford. The full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/10%20PRESENTACLON%20DE%20SALMON%20AQUADVANTAGE.pdf

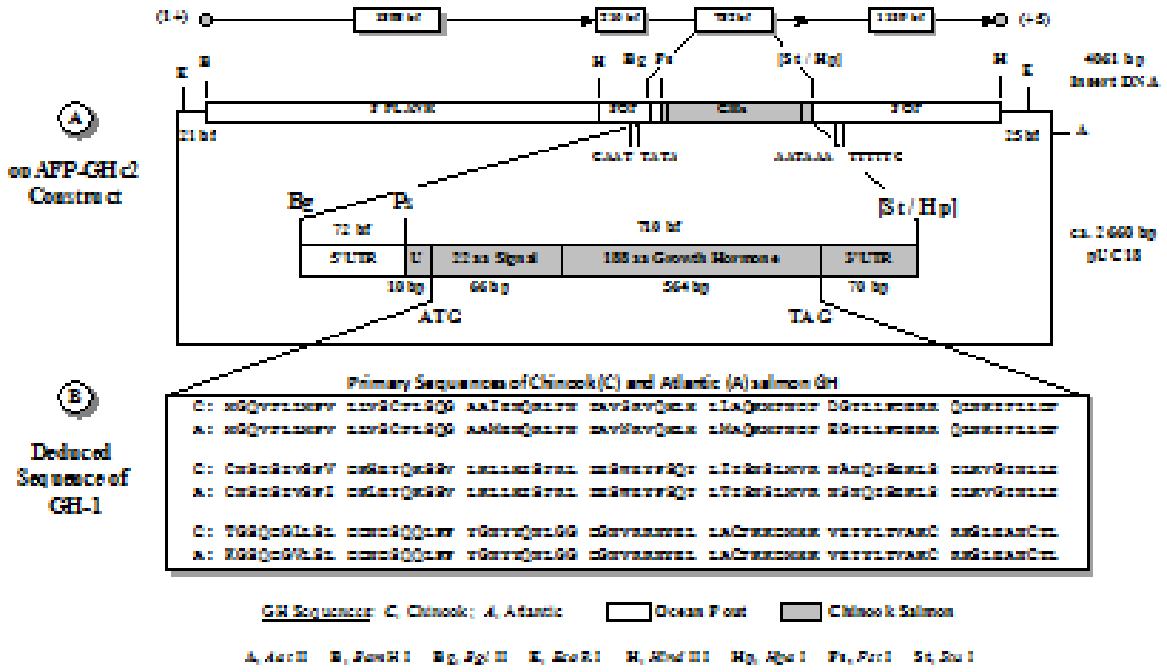

Figure 8. Physical description of the *AquAdvantage*® transgene (opAFP-GHc2).

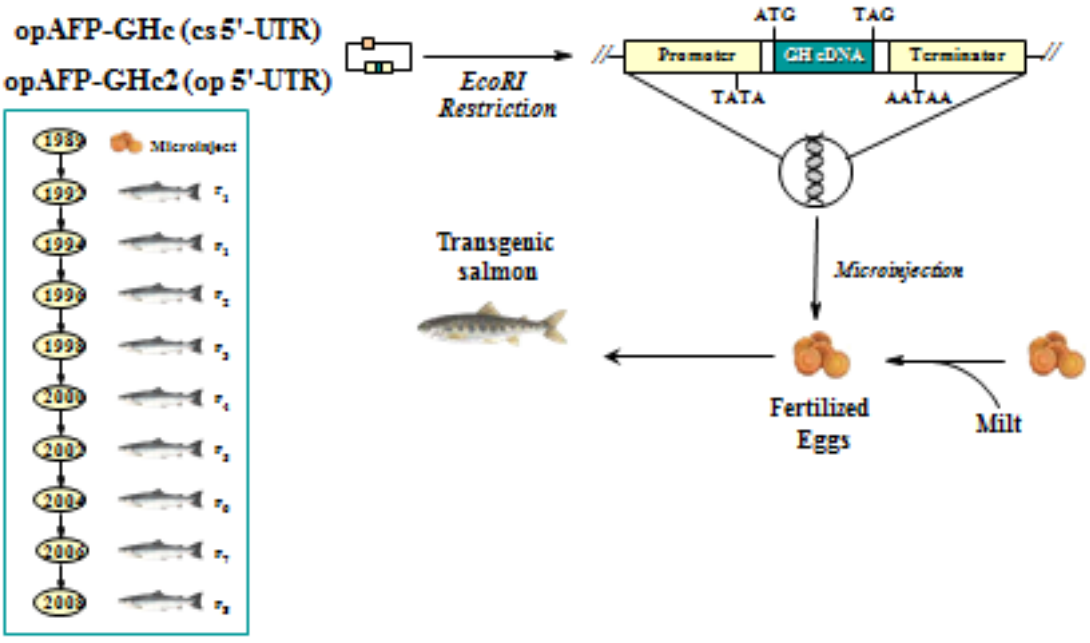

Figure 9. Heritability and durability of the *AquAdvantage*® transgene.

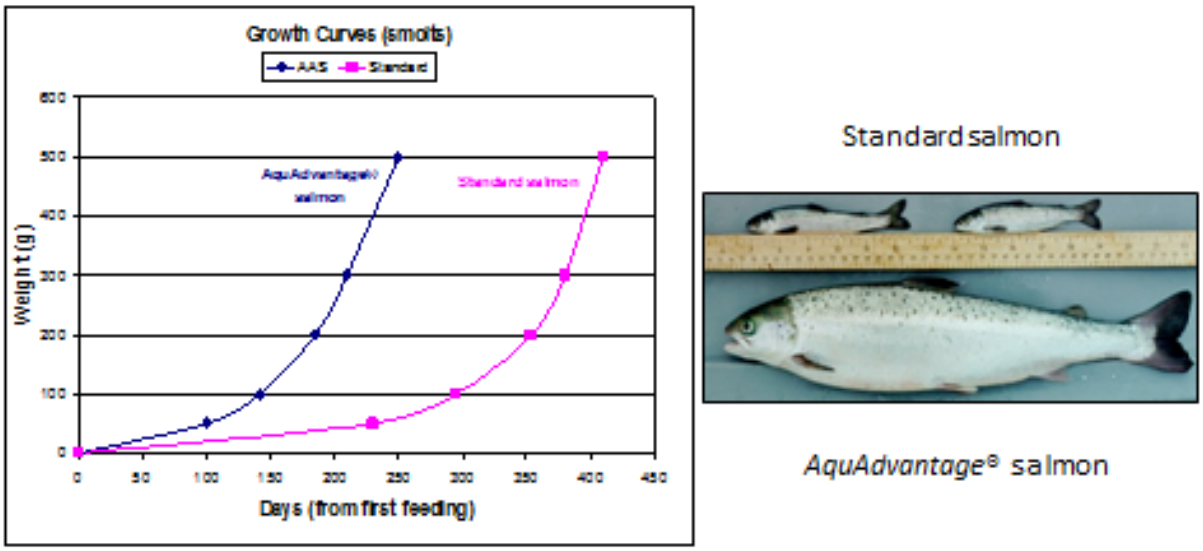

Figure 10. Superior growth rate in *AquAdvantage*® salmon.

If approved by the U.S. FDA, AquAdvantage Salmon will have a very specific regulatory definition and strictly imposed conditions of use. In order to minimize the potential environmental risk, the FDA has imposed several conditions of use on the AquAdvantage Salmon. AquAdvantage Salmon will not be permitted for culture in floating sea cages (which is the traditional method for farming salmon, but instead will be limited to land-based, freshwater, contained culture systems. Due to the excellent growing conditions for salmon, a tradition for aquaculture pioneering, and a pro-biotech regulatory environment, Panama was chosen as a suitable site for R&D and the experimental production of AquAdvantage Salmon. A site in the highlands of Panama was selected, inspected, and approved by the FDA as a growout site suitable for production and export (to the USA) of AquAdvantage Salmon, once FDA approval and local Panamanian regulatory approval is granted. Until such approvals are granted, the Panamanian growout site is only authorized only to conduct R&D with AquAdvantage Salmon, and all fish produced at this site must be sacrificed and destroyed (buried) at the conclusion of each experimental cycle (Fig. 11).

Figure 11. For regulatory reasons, the fish are slaughtered and destroyed at the end of each experimental cycle.

The AquAdvantage Salmon produced at the Panama site are sterile and all-female, assuring that reproductively active, self-sustaining populations cannot be established at the site or in the environment, nor could the experimental animals breed with other wild fish. The Panama site is equipped with a total of 21 individual physical containment barriers designed to prevent the experimental fish from escaping into the environment. These barriers consist of screens, filters, nets, bag nets, containment sumps, etc. (Fig. 12).

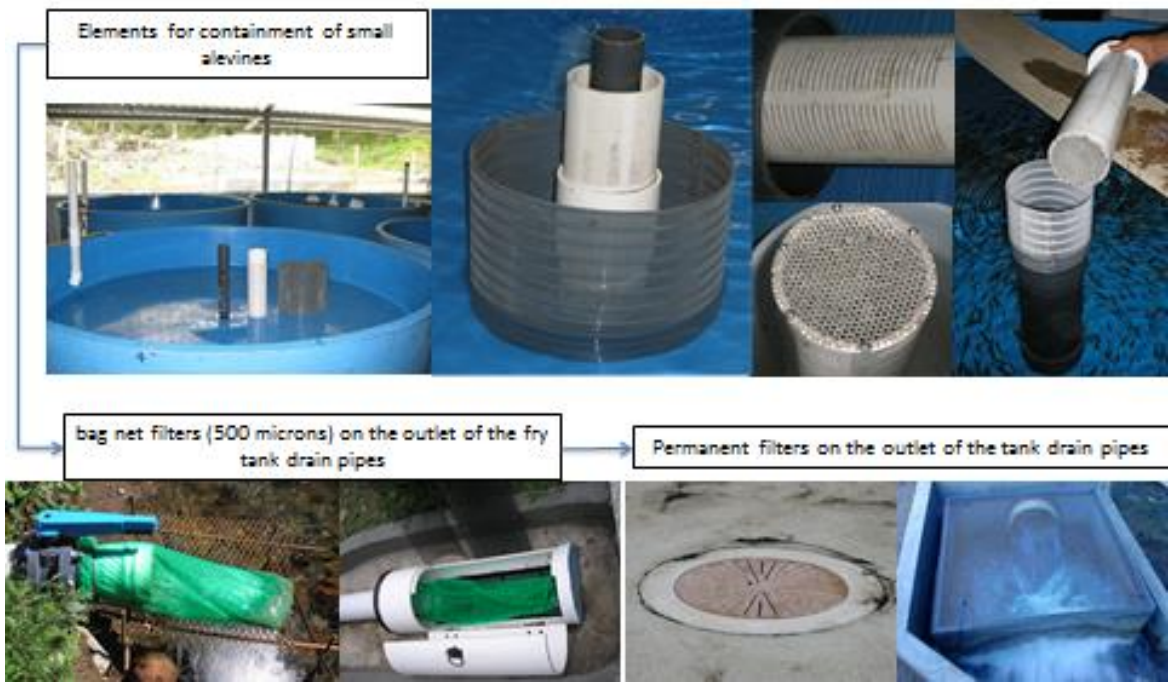

Figure 12. Physical containment barriers.

In addition to the 21 physical containment barriers confining the experimental fish to the culture system, downstream from the project there are numerous hydroelectric plants, as well as a natural (ecological) thermal barrier of lethally high water temperatures that would prevent any live salmon from reaching the Pacific Ocean. In conclusion, there are a large number of layered, redundant biological, ecological, and physical containment barriers in place at the Panama site, which considerably minimize the environmental risk.

It is very likely that the AquAdvantage Salmon will be the first genetically modified food animal to receive regulatory approval due to the numerous containment measures built into the AquAdvantage Salmon and its intended production system, due to the fact that AquAdvantage Salmon has been determined to be equivalent nutritionally and biologically to a conventional farmed Atlantic salmon, and due to the fact that it has been determined to be safe for the environment and safe for the consumer.

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4.2. Regulatory aspects in genetic modified animals[9]

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The case of genetically modified animals in Argentina

Since 2007, Argentina has striven to address the rise of biotechnology in animals – specifically, the livestock sector. The objective behind this effort was to prevent the same errors made with plant biotechnology, which were attributed to a general lack of insight pertaining to GM crops.

Initially, the cloning of livestock was considered and applied to animal biotechnology, leading to a period of significant technology development within the country. In anticipation, Argentina proceeded to establish an appropriate regulatory system prior to accepting applications from stakeholders.

Various training sessions were held as part of this framework, such as the *First International Workshop on the Food and Environmental Safety Assessment of Genetically Modified Animals,* held in September 2011 under the auspices of the International Centre for Genetic Engineering and Biotechnology (ICGEB) and the Biotechnology Program for Latin America of the United Nations University (UNU-BIOLAC).

The aforementioned event included 120 participants from 30 countries and five continents who spent a week reviewing experiences and current guidelines as part of discussions held on regulatory matters pertaining to genetically modified animals. The first day included a review of the latest engineering achievements in animals and associated biotechnology activities, such as cloning or so-called non hereditary technology. On day two, we surveyed the current developments and gaps in environmental risk assessment of transgenic animals. Day three involved a broad coverage of safety assessments. Day four addressed non-technical matters associated with biosafety such as its socioeconomic and ethical implications. Field visits were carried out on the final day.

Assessment of environmental biosafety

Although information is available with regard to environmental assessment of GM animals, it refers to specific cases of GM animals. For example, GM fish (Aquabounty case), GM mosquitoes (Oxitec case), and guidelines of the World Health Organization (WHO) and PCB. In addition, there are EFSA guidelines for fish, mammals, birds and insects that have been starkly criticized for allegedly being too theoretical and difficult to put into practice.

[9] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/11%202013-02-28%20animales%20MLema.pdf

Argentina has set precedents and disseminated information for safety assessment in GM animals. For example, the information provided addressed assessments performed on GM cattle in confined areas in the country. In addition, countries such as Cuba, Panama and Malaysia have also provided data on their research performed on GM fish.

The FDA´s assessment of GM salmon may be considered to be an exception. The assessment was executed in two stages. The first stage was carried out according to *Codex Alimentarius* guidelines and is considered to be very solid. A second stage, which was recently published as a biosafety assessment, is regarded as being rather unusual, given that the FDA has performed a safety assessment on salmon that is not cultivated in the United States, an assessment that experts have referred to it as being technically viable, yet, superfluous.

Harmonized risk assessments are an ever-present topic in every country that performs risk assessments. This need also applies to GM animals since different focuses emerge with different procedures and objectives.

The need to perform assessments according to each animal species or type has also been considered, given the relevant differences considered in biosafety, such as animal use, its capacity to escape or reproduce beyond human control, the environment in which it interacts, etc.

It is necessary to establish containment methodologies within the guidelines for biosafety assessment in GM animals, since there are many constraints associated with animal confinement. Animals need to be housed in confined areas in order to obtain the desired results and prevent GM traits from being released into the environment.

It is also important to bear in mind that episomal elements (retrovirus sequences, for example) are commonly used in the development of certain GM animals and are favored by breeders since they facilitate genetic transformation. But, since most GM breeders have worked in academic surroundings without anticipating the possible questions that would be raised by regulatory authorities, their biosafety assessments did not address cases where genetic elements could migrate and separate from the genome where it was originally located.

Consequently, some breeders have proposed that GM animal assessments focus on traits introduced in combination with the species. This is different from GM plants, which are assessed on a "case-by-case" basis – in effect, event by event. Such a development would be a real change in the paradigm used for GMO assessments in the past.

The assessment of food safety

The guidelines of the *Codex Alimentarius* are regarded as robust precedents for food safety assessments of GM animals, given that the process of drafting them involved a great deal of government interaction and they have been in place for a long time. The conclusion is that the assessment objectives and procedures will not be very different from those that are now the norm for GM plants.

For example, one of the most conspicuous differences between the guidelines for the assessment of GM plant and animal-based foods is that the guidelines for animals rule out gluten sensitivity analyses (since gluten is not found animals). The conclusion, then, is that since there are no

major differences between the guidelines, the development of functional regulatory frameworks for GM animals is likely to be faster than in the case of GM plants.

A watershed in relation to safety assessments in GM animals is the Aquabounty salmon case, the first GM animal that has undergone the complete safety assessment approval process for human consumption (FDA assessment).

An issue that has recently come to light with regards to GM animals is modification by companies of animals not fit for human consumption (for example, a drug that is produced in milk) and then subsequent use of those animal byproducts (for example, use of meat for human consumption). The challenge lies in developing regulatory frameworks that include safety assessment clauses for byproducts from genetically modified animals with traits not associated with human consumption.

Non-hereditable technologies, such as gene therapy in animals or gene insertion in an adult animal (or one that is not an embryo), so that cells may produce a protein of interest (treatment hormones for the animal itself or antigens for vaccinating the animal), may lead to the modified cells becoming part of the tissue of the animal that is then used for human consumption, even though the modification is not inherited by the animal's offspring. This raises issues that would have to be considered with regard to safety assessments.

The related issues that do not form part of the risk assessment but are important for the decision-making process and the social and political acceptance of GMO policies include bioethical considerations, communication, socioeconomic aspects and labeling, among others.

With regards to bioethical concerns, genetic modification is allegedly performed on animals considered to be sensitive creatures; all possibilities for genetic modification to affect an animal's wellbeing must be analyzed using the same criteria applied to other factors that may modify the animal's condition that do not originate from genetic modification. All of these considerations should then be addressed when decision-makers voice their support or rejection of any technology.

Other bioethical issues that may arise include topics that impact public perception or acceptance. There is a need for dissemination campaigns that do not polarize opinions. Experience has already been acquired with transgenic plants, about which public opinion is divided. The social and environmental benefits of their use also need to be analyzed and disseminated.

Some examples of GM animal research throughout the world include:

- University of Guelph, Canada, with swine that express phytase in saliva so that they may use phosphorous present in maize instead of having to add phosphorous to their diet. As a result, their excrement has a lower amount of phosphorous, which, in turn, reduces environmental pollution caused by non-GM swine. Unfortunately, after years of development and proof that this technology actually works, the animals were sacrificed for lack of a viable operational regulatory system that could be implemented in the market.

- Developers at the University of California-Davies, in the United States, developed goats that expressed human lysozyme in milk.

- Argentina: The National Agricultural Technology Institute developed cows capable of producing lactoferrin and human lysozyme for nutraceutic use. The company, BioSidus, developed cows that produced the human growth hormone and insulin in milk to be used for purification and pharmaceutical purposes.

It is important to mention that China is perceived as the country with the greatest development of transgenic animals, having developed enhanced biotechnology versions of the pioneer examples from other countries; and more recently, new events for different types of transgenic animals with extremely varied and novel traits.

Analysis and sampling methods in GM animals

Sampling methods contrast notably with the more familiar methods used for GM plants since the genetic traits are very different for each construction. Although initially GM animal development was more customized and based on the individual results of researchers who produced GM animals from scratch, genetic traits could not be used interchangeably, so the same promoter or terminator could not be used. Each construction is unique and each transgenic animal will, most likely, require its own detection method. There will be no universal methods of detection. In addition, it has been found that the matrixes are more diverse (milk, meat, egg, captured insects, etc.), which makes it more necessary to develop DNA or protein extraction methods on a case-by-case basis.

Conclusion

It is necessary to continue to develop regulatory capabilities for environmental and food safety assessments in transgenic animals. Today, regulators are more knowledgeable about technologies associated with transgenic plants, providing them with a solid base for creating new capabilities. It is also important to learn from past experiences in regulating GMOs, particularly as regards the need for more fluid interaction among regulators, developers and society that makes it possible to anticipate the issues that are likely to arise.

4.3. Discussion panel on risk assessment and GM animals

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Speakers: Edith Vargas (Panamá), Martin Lema (Argentina)
Moderator: Pedro Rocha (IICA)

4.3.1. GM Animals

There are several points to consider with regard to the question of using animals as bioreactors versus mammalian cell cultures:

- If a biologically active protein can be obtained from an animal (in milk or eggs), it would be less expensive to use animals rather than cell cultures. .
- The preference for one or the other often depends on the research endpoint itself, since the situation may arise where the protein requires folding that can only be obtained by cell culture.
- However, the use of animals as bioreactors appears to be more complex, because more permits have to be obtained. That calls for more expeditious, but no less stringent, regulatory frameworks

Argentina's management of GM animal by-products required destruction of all materials after completion of activities and, as a result, all GM animals were slaughtered and buried. So far, there has been no proposal or request for by-product utilization that is considered to be a temporary measure. In the future, as this activity grows, the same breeders are bound to request permission to use such products. The same thing occurred with GM crops: initially, the GM maize by-products were not used but breeders have gradually requested permission to use the by-products to produce the biogas used in seed production activities.

When the term, "cisgenesis" began to be promoted, its supporters argued that cisgenics were different from transgenics, since the former were first transformed with a gene from their own organism and, if the organism had a history of safe use, it was assumed that all of its proteins were safe and did not require a risk assessment. This argument is not valid if one performs a case-by-case analysis. For example, certain plants express proteins involved for self-defense which are only produced under stress and are toxic for human beings (lectins, for example). If a gene is used to express these proteins and provide the plant with a greater degree of protection, even if the genes belong to the actual plant, any food derived from this plant would potentially be more dangerous.

To conclude, cisgenics should be regulated like transgenics because they fall within the definition of a GMO (an organism that receives a man-made genetic construct). Also, since this new cisgenetic construction may induce an increased amount of protein, it may make the food toxic and allergenic and pose new risks.

4.3.2. GM Salmon

GM salmon aquaculture versus its non-GM equivalent is considered to be more environmentally friendly, since deep-sea fishing for non-GM fish uses nets. When salmon are fished with nets, a large quantity of salmon is caught that are not of the required size, as well as other species. Since GM salmon is confined, there is complete control of the process and only GM salmon are fished.

According to GM salmon aquaculture protocols, the process must initiate with "eyed eggs." The initial growth stage (fry stage, until they weigh 500 grams) is the greatest growth period for salmon. During this stage, their diet is a critical control point. Several trials have been executed with different diets with feed produced by Panamanian companies. However, the composition of the diet is classified information.

The Panamanian authorities have conducted several monitoring activities for GM salmon farming. Various visits have been made to inspect the salmon tanks. Specific emphasis has been placed on:

- How the fish are removed and verification of the amounts reported, to confirm that the numbers match the amount of salmon subsequently disposed of.
- Adherence to procedures for proper disposal of animals (burying, adding of lime, etc.).

It is considered that the GM salmon farming cannot be conducted in the U.S. or Canada, since the Atlantic salmon is native to these countries, which is a risk if the GM salmon were to accidently escape. If this were to occur, GM salmon would run a higher risk of breeding with wild Atlantic salmon. The objective of this project is to produce Atlantic salmon outside of the United States, in this case in Panama, and import it fresh, filleted, packed and ready to be introduced to supply chain restaurants.

If the salmon were to be sold for human consumption within Panama, the correct procedure would be to submit an application to the ANC that would be used to perform a risk assessment. The Biosafety Committee performs the final assessment to approve or ban it from being consumed in the country.

These types of salmons are cisgenic salmon, as they have been modified with a gene from the same organism.

Three countries are involved in the process of developing GM salmon: Canada produces the eggs, Panama grows the salmon and the United States consumes the finished product. Although information has been freely exchanged among the three counties, gaps have been encountered and meetings have been held to clarify data and discuss the reasonable doubts related to safety.

It should be emphasized that if, during the GMO approval process, doubts are expressed about the information or the data is incomplete, there must be mechanisms in place to ensure that the information reaches the decision makers, so that the decision to approve or reject an application is well founded.

Section 5: Risk Assessment in Environment and Health

5.1. Regulatory Aspects for GM Mosquito Release in Panama[10]

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Panama has experienced a rise in dengue fever during past few years along with the proliferation of its vector agent, *Aedes aegypti*, particularly in urban areas. In 2011, the Gorgas Memorial Institute for Health Studies (GMI), in collaboration with the private sector (the English company, Oxitec), asked Panama's National Commission to carry out a study of genetically modified mosquitoes.

The main objective of this project was to perform controlled studies where local experts released genetically modified male mosquitoes so they could breed with wild females (which had not been modified) and thus endeavor to reduce native vector populations in the metropolitan area and, ultimately reduce dengue fever, a painful and sometimes lethal disease.

The technology assessed, developed by Oxitec, consists of a strain of *A. aegypti* mosquito (referred to as OX513A) that is a homozygote. Two expressible genes are then inserted. One of these genes is referred to as a *fluorescent marker*, which expresses a fluorescence marker. This is a "conditioned" lethal gene system referred to as the "lethal system" where mosquitoes develop a protein that ultimately kills them, unless the larvae are fed with a tetracycline that represses the expression of this lethal gene.

The research project comprises two stages. The first stage is the rearing stage, which involves screening of males and females, assessment of competitiveness and breeding of the GM mosquitoes. During the second phase, the GM mosquitoes are released and effectiveness monitoring efforts are undertaken. An application must be submitted during each stage of research for consideration and assessment by the Sectoral Committee on Biosafety Health (CSBS), and its recommendation must be approved by Panama's National Biosafety Commission. The CSBS is still evaluating and reviewing the technical documentation for this application to approve GM mosquitoes, which includes the technical dossier presented by Oxitec and assessments performed by Malaysia and Brazil regarding this technology.

As this authorization and assessment process is under way, the ICGES has begun to refurbish its facilities (insectaries), assess and select the areas where the studies will be undertaken, and train its technical staff to ensure that this technology is effective and does not pose a health risk for the population and the environment.

[10] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/12%202013-02-28%20CRC%20Aspectos%20Mosquito%20LBenavides.pdf

5.2. Biotechnology in 2012: Maize, cancer and rats[11]

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Genetic modification is a biotechnology technique that, in recent years, has greatly impacted and generated discussion in the agricultural sector. Controversies concerning genetic modification (GM) include environmental, human/animal health, economic, legal, political, social, and philosophical issues. Although broad, unbiased and accurate discussion is an important initiative, since it leads to the debating of ideas, acceptance of facts or rebuttal of interpretations, issues surrounding GM crops continue to be imbued with a pervasive blend of pseudo-scientific arguments and assumption-based interpretations. This debate has led to public distrust of biotechnology and unfounded statements that create confusion (SIMAS, 2009) and attack this important and useful technology for improving agricultural performance and safeguarding farmers' well-being.

Since the emergence of GM crops for food and feed (particularly soybean and maize), controversies have surfaced with regard to the safety and regulatory aspects of GM-derived food products. The main concern that has surfaced (though reasonable and valid) is whether these types of products adversely impact human or animal health. In an effort to respond to this query, expert groups have performed rigorous scientific experiments published according to strict assessment protocols conducted by external peer experts. There is a vast number of scientifically validated studies (as reviewed by Herman & Price 2013) with significant findings in defense of GM crops and, currently, no scientific publication has published a report stating that GM maize or other GM crops sold on the global market have harmful effects on human or animal health.

Nevertheless, rigorous scientific studies contrast sharply with the flippant inferences originating from semi-scientific experiments and even conclusions based on non-commercial events. So-called researchers have carried out biased experiments that clearly violate the postulate of objectivity and the rigor of science. Unfortunately, the lack of appropriate outlets prevents analysis of false, biased or mal-intentioned reports that are generally available in non-peer reviewed journals or on the Internet and lack scientific-technical criteria. The following section addresses one of the most well-known examples of such a report, which falsely alludes to the damaging effects of GM maize on animal health (Seralini *et al*. 2012).

Essentially, the hypothesis reported by Seralini *et al*. (2012) for this study involved testing whether GM maize (NK603 glyphosate resistant) affected the onset of cancer in rats. The experimental design involved (Fig. 12) feeding Sprague Dawley rats (males and females) four treatments (diets): 0%, 11%, 22% and 33% of GM maize. Ten rats were used for each treatment. In addition, the study included a supplementary diet of three doses of glyphosate: 50 mg/l, 400 mg/kg and 2.25 g/l. The animals remained in the experiment for two years (central premise of

[11] Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/14%202013-02-28%20CRC%20PRocha.pdf

the experiment). The response variables were based on microscopy and pathology studies, supported by a new multivariate statistical analysis system.

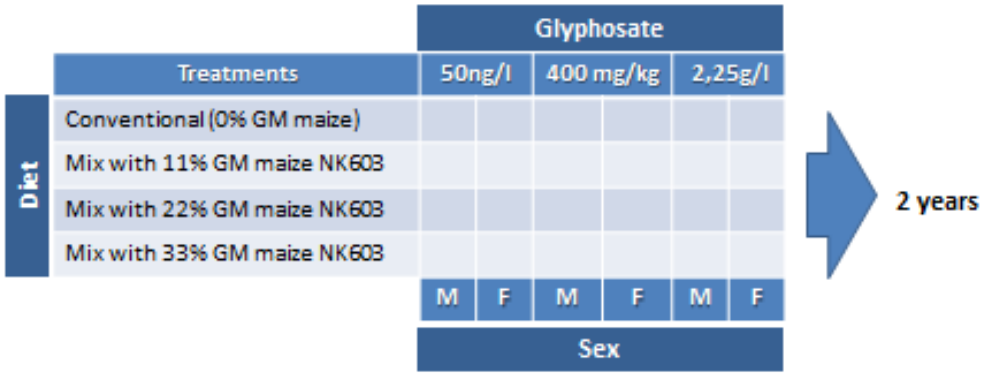

Figure 12. Experimental design summary of results presented by Seralini *et al*. (2012)

Seralini's findings can be summarized as follows (Seralini *et al*. (2012)): (i) lower levels of glyphosate at a concentration below officially set safety limits induce severe mammary, hepatic and kidney problems; (ii) the disruption of biosynthetic pathways that may result from overexpression of the EPSPS transgene in GM NK603 maize may lead to comparable pathologies, (iii) other mutagenic and metabolic effects of edible GMO cannot be excluded and could be explained by the overexpression of the transgene in GM.

After careful analysis of the experimental design and the results presented, the peer-review consensus[12] is that the conclusions of Seralini *et al.* (2012) have no validity. It has even been suggested that the article be retracted (Tien & Huy-FCT, Grunewald-FCT 2013) given its unacceptable experimental design errors, serious deficiencies in its protocol, procedures (Wager-FCT 2013) and statistical analysis (Ollivier-FCT, Panchin-FCT 2013), and in the interpretation of the results. As a result, Seralini´s conclusions are invalid (Sanders *et al*.-FCT 2013). In addition, the *sui generis* opaque style and lack of scientific ethics of the authors of the study in presenting their results is questionable (Macedo-Souza-FCT, Grunewald-FCT, Montagu-FCT 2013).

The arguments in question challenge the technical rigor of the article and the lack of scientific quality attributed to the study, which is detailed in the following examples:

(i) Sprague Dawley rats were used in a two-year experiment to test the onset of tumors during a two-year period (104 weeks), although it has been known for many decades that these types of rats developed tumors prematurely (from week 13, Prejean *et al*. 1973). It is evident that Sprague Dawley rats were not adequate subjects for this study, as was recently demonstrated by an independent group (Hardisty *et al.* 2013).

(ii) The rats were fed increasing concentrations of glyphosate and the experiment did not monitor water intake.

(iii) The classical statistical test for mortality rate comparisons in various treatments is the Chi-square. Yet, this data was not reported by Seralini *et al.* (2013) (Ollivier-FCT 2013).

[12] The scientific concept which refers to "hundreds of researchers" is featured in the "Letters to the Editor" section of the journal *Food and Chemical Toxicology* (2013), Vol. 53, P. 440-483. In order to maximize space, this article does not use the traditional style for references but, rather, cites the author and initials of the journal (FCT).

Furthermore, the study reports that 30 different organs per animal were analyzed. However, only a few of those organs were actually shown. This creates a statistical problem for multiple comparisons, which the article never mentions (Panchin-FCT 2013).

(iv) The results do not explain why more rats die in control experiments than during treatments. In addition, the mortality trends do not distinguish between the effect of the type of rats, the effect of the glyphosate and the effect of the different concentrations of GM maize.

(v) The inclusion or scientific relevance of including explicit photographs of rats with tumors in the paper is unclear. The potential media stir that can be caused by the photographs contrast sharply with the poor quality and simplistic nature of the statistical data presented.

(vi) The peculiar manner in which the authors managed the communications and dissemination aspect of the study was a highly unusual strategy for a scientific researcher, and seemed to be designed more to make an impact in the media than to communicate scientific findings. Also, pre-publication access to the paper was only granted after signing an openly restrictive confidentiality agreement that prevented journalists from obtaining comments from other third-party scientists (Montagu-FCT 2013).

The aforementioned observations are taken from the dozens of scientific questions submitted by the international scientific community (FCT 2013). Another comprehensive review can be found in Arjo *et al.* (2013).

The irresponsibility that characterized the erroneous conclusions drawn that resulted from the study's poor experimental design and statistical analysis, led to a biased and heated debate to which the international scientific community responded unanimously. This resulted in an improved oversight and rigor of the peer review system. These positive results, however, were dampened by the negativity and fear that was instilled among the public at large. Such a perception could eventually jeopardize food security among certain vulnerable populations. Another damaging result was the resulting public distrust of the scientific community and its objectivity and the journal's scientific credibility was challenged. It also disqualified the various assessments and scientific analyses that had been executed by the countries' biosafety commissions that had authorized GM crops to be planted, and led to hasty approvals to implement vetoes or moratoria against transgenic technology in some countries, as well as economic effects (such as the partial ban on imports, disruption of trade activities in the market, etc.).

One final comment on the GM maize debate. There has been no experimental finding suggesting that GM maize or any other GM crop marketed anywhere in the world is harmful to human or animal health and the environment.

Though technology is developed based on its potential contributions, it is overestimated or underestimated as a result of ignorance. Scientific ethics, human audacity and regulatory frameworks lead to the responsible use of technology and even make it possible respond to unforeseen consequences. This has been a constant throughout the history of humanity. But it is, precisely, due to such behavior that advances are achieved and problems solved. However, scientific objectivity is challenged by publications such as that of Seralini *et al*. (2012). For this reason, the scientific and technology community has an obligation to ensure rigorous and quality scientific research, and to call out and censure anyone who deviate from the principles of scientific integrity. IICA defends that stance.

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5.3. Discussion panel on risk assessment in environment and health

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Moderator: Jorge Madriz (Costa Rica)

5.4.1. GM Mosquito

Only male mosquitoes undergo genetic modification, and research has shown that females do not have a preference for one over the other (i.e., GM over non-GM, or vice versa). In principle, GM and non-GM males are the same; the only difference is that GM mosquitoes have a fluorescent glow when placed under a UV lamp.

Experiments were conducted with GM and non-GM males placed at opposite ends of an enclosed space. Females were released and analyzed to determine whether they were more attracted to one or the other. In fact, the males sought out the females and the GM males were not rejected by the females. Thus, the male's ability to fly is the decisive factor in controlling the mosquito population.

The frequency with which GM mosquitoes should be released into the environment was determined to be once a week. The mosquito population is not eliminated entirely in that lapse of time, however, as there are always areas that the GM mosquitoes do not visit. Nonetheless, the mosquito population was reduced significantly for approximately two to three months.

An important argument against the use of these GM mosquitoes is that scientists do not understand the molecular mechanism whereby mosquitoes die after activation of the specific protein produced by the gene (lethal system) controlled by the tetracyclines. This has been criticized by opposition groups, which argue that the insects could suddenly develop a natural resistance (which is possible, but has never been observed). It would be much better if the molecular mechanism were understood, but the absence of the information should not prevent the mosquitoes from being used. Many vaccines were used long before their working mechanism was understood.

The question of which national agency should regulate GM mosquitoes in the different countries of the region is still under discussion, as a number of issues need to be clarified and several decisions taken. For example, some health authorities affirm that mosquitoes are animals and, as such, do not fall within their remit. Others say that GM mosquitoes propagate dengue fever and are a public health risk. The conclusion to be drawn from all this is that the time has come to create intersectoral groups to regulate these and other GM organisms that will be developed in the future, because their impact will be felt across different sectors.

Section 6: ICABB

6.1. Initiative for Central America on Biotechnology and Biosafety (ICABB)[13]

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The Central American Initiative on Biotechnology and Biosafety (ICABB) is a regional group comprised of the directors / chairs / executive secretaries of the national technical commissions on biosafety (CTNBios) of Central America (Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama and the Dominican Republic) or, in their absence, of the national biosafety regulators.

The ICABB aims to bolster actions at the national and regional levels designed to ensure access to biotechnology, the safe use of its products, and the optimization and harmonization of the legal and policy frameworks for biosafety. As well as placing such actions on a formal footing, the group's ultimate objective is to boost agrifood systems, improve the quality of rural life, protect the environment and strengthen economies.

The ICABB's strategies

Following national and regional consultations, it was decided that the initiative should focus on the following four strategic areas:

a) Policies and the legal framework
The success of biotechnology stewardship is contingent upon technical and scientific knowledge, direct strategic planning actions, negotiation, socio-economic considerations, financial management, biosafety, intellectual property rights and other factors. Therefore, a regional policy on biotechnology and biosafety is critical to foster the construction or strengthening of legal frameworks to address the issue.

b) Public perception, education and information
Good biotechnology management may be overshadowed by poor public perception of the issue. The ICABB needs to devote special attention to raising awareness and educating a wide range of social groups on the subject, to instill a better and more objective perception of biotechnology.

[13] This presentation was given by Pedro Rocha and the text was a contribution from Bryan Muñoz. Full presentation is available at http://www.iica.int/Esp/Programas/Innovacion/Documentos%20de%20Tecnologa%20e%20Innovacin/00%202013-02-25%20CRC%20ICABB%20PRocha.pdf

c) Enhancing institutional capacities in biotechnology and biosafety
The autonomy of the countries and regions in the area of biotechnology will depend on the creation and strengthening of the technical, human and institutional capabilities required to establish and implement local and regional research and development agendas. This initiative will also give the countries a platform for exchanging information on biotechnology and biosafety that will enhance local capacities throughout the region.

d) Biotechnology research, innovation and commercialization
A regional biotechnology initiative should promote the development of the bio-economy by establishing links between laboratory research facilities and industry. This could be achieved by creating platforms for technology development, identifying opportunities for the creation of biotechnology companies, pinpointing business opportunities and building capabilities in this field.

Conceptualization and Creation of the Group

From 2008-2011, the Inter-American Institute for Cooperation on Agriculture (IICA) conducted a survey to assess the current state of biosafety in the region (IICA, 2008). In 2011 and 2012, the biosafety authorities of several countries in the region took part in the project, "Latin America: Building Multi-Country Capacity for the Implementation of the Cartagena Protocol on Biosafety" (LAC-Biosafety), which highlighted the importance of joint efforts, particularly in the area of biosafety research.

At the LAC-Biosafety meeting held in June 2011, the Central American countries proposed that IICA assist them in setting up a regional working group to oversee the region's biosafety interests and integrate the results of the UNEP-GEF biosafety projects under way in several countries. In March 2012, a workshop was held in Panama City for members of the CTNBios in Central America, who discussed the needs of the countries and the possible creation of a discussion and working group. The delegates endorsed the idea of setting up a formal consultative group on biosafety for the region, and charged IICA with making the necessary arrangements. All these efforts were consistent with IICA's 2010-2014 MTP.

In May 2012, the International Conference on Agriculture and Environment (ICAA) was held at Zamorano University in Honduras. The participants discussed the possibility of setting up a broad group of biosafety experts from the Central American countries to stimulate discussion of the issue and put forward ideas. The group could also provide technical advice to the ICABB.

During meetings held in September and October 2012, in Argentina and India respectively, calls were made for Central America and the Dominican Republic to establish the ICABB by signing a formal document for its creation in the near future. IICA was tasked with facilitating the process. It was also decided that country membership of the group should be voluntary and not affect the national provisions of each member country.

In a formal ceremony hosted by the Director General of IICA, Dr. Victor Villalobos, delegates from all the Central American countries and representatives of the Costa Rican government signed the document for the creation of the ICABB at IICA Headquarters in San Jose, Costa Rica on February 25, 2013 (Annex 3).

Internal Organization

The group is composed of the directors, chairs and executive secretaries of the CTNBios of Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama and the Dominican Republic. In the absence of a formal or organized country commission, the member may be nominated by the interim national commission or, if none exists, by the competent national authority on biosafety (or whomever the commission or authority designates as its representative). Each CTNBio also appoints an alternate delegate to attend all ICABB meetings if the regular delegate is unable to do so. The alternate delegate has the same rights and obligations as the regular delegate.

If a topic to be addressed at an ICABB meeting is scientifically very complex, each country may appoint an expert representative or group of representatives to address that issue as a commission. The ICABB may also unanimously appoint an expert or group of experts outside of the region to serve as technical advisors for the specific issue.

In order to tap into the expertise available and promote horizontal cooperation within the region, the ICABB may invite observer countries that express their intention of participating in the processes, with the right to speak but without the right to vote.

The ICABB's activities are managed by a General Coordinator, a Technical Secretary and an Assistant Coordinator. These positions are voluntary and the holders are elected by the group. The responsibilities, rights and duties of these positions are established in the ICABB's general regulations. The steering group has a Support Unit that convenes meetings and facilitates the ICABB's work, but does not have the right to vote. The ICABB appointed IICA as the Support Unit, given its commitment to, and experience and cooperation in, biotechnology and biosafety work for the region. However, this position is not permanent and it is up to the ICABB to decide which institution will support its activities.

The ICABB's decisions and projects

The founder members of the Central American Initiative on Biotechnology and Biosafety (ICABB) met at IICA Headquarters in San Jose, Costa Rica on February 25, 2013 (see Annex 2). The meeting was attended by Eugene Waight (Belize), Alex May (Costa Rica), Jeremías Yanes (El Salvador), José Mauricio Hernández (Guatemala), Carlos Almendares (Honduras), Jorge Garcia (Nicaragua), Ivette Vargas (Panama), and Marina Hernandez (Dominican Republic). The meeting was led by Bryan Munoz of IICA, in his capacity as Acting Secretary.

The business of the meeting was divided into two parts. First, the participants focused on administrative and organizational matters, including the rules governing the voting process, the procedure for submitting proposals, and the first elections of the officers of the steering group. The results of the election were as follows:

Alex May (CTNBio, Costa Rica)	General Coordinator
Eugene Waight (CTNBio, Belize)	Technical Secretary
Mauricio Hernández (Intersectoral Commission, Guatemala)	Assistant Coordinator
Bryan Munoz (Area of Biotechnology and Biosafety, IICA)	Support Unit

It was also decided that during the first period of operations the Steering Group would draw up the operating rules of the ICABB and the procedures that will govern future actions.

In the second part of the meeting, the participants addressed the initial lines of action on which the ICABB would focus. Prior to the meeting, the Acting Secretary had drawn up a medium-term action plan based on the strategic areas already established by the countries. The group was asked to present results from these lines of actions at the next ICABB meeting, to be held within the next two years.

Action 1 Prepare a document on the state of the art of biotechnology and biosafety in each country of the region.

Action 2 Establish a support group on issues related to the Cartagena Protocol to provide the countries with a technical foundation on which to prepare their national positions for the COP-MOPs. It was decided that the first step would be to provide follow-up to the group negotiations on socioeconomic considerations in the context of the CPB.

Action 3 Establish a technical support group that will report to the CAC, CCAD, COMISCA, CAS and NABI on the ICABB's activities and the advances made in biotechnology and biosafety in the countries.

Action 4. Establish a regional biotechnology information/documentation system. This virtual platform will be used to make the ICABB's decisions public.

Action 5 Lay the groundwork for a regional project with the UNEP-GEF, respecting that organization's procedures and taking into consideration the national priorities of the ICABB's members.

The information included in this section is referenced in the ICABB-001 Minutes.

Thus, the ICABB is an example of regional integration on specific issues pertaining to biotechnology and biosafety.

Reference

Inter-American Institute for Cooperation on Agriculture, IICA. 2012. Iniciativa Centroamericana de Biotecnología y Bioseguridad: Hacia el desarrollo de un mecanismo regional. Technical Coord. B Muñoz, P. Rocha. San Jose, CR, IICA.

Section 7: Workshop Description, Program and Participants

7.1. Description of the Workshop

7.1.1. Background

- AB&B-IICA has become a go-to institution for the technical capacity building required to create and implement biotechnology/biosafety policies and institutions in Latin America.
- The National Biosafety Commission (CTNBio) of Costa Rica is currently participating in a biotechnology project funded by UNEP-GEF aimed at biosafety capacity building.
- IICA facilitated the creation of the Central American Initiative on Biotechnology and Biosafety (ICABB), which held its first official meeting on February 25, 2013 at IICA Headquarters in Costa Rica.
- IICA, UNEP-GEF and ICABB proposed the Workshop on Risk Assessment in Biosafety, aimed at regulators, policymakers and other stakeholders involved in risk assessment processes in Central America and the Dominican Republic. Regulators from other regions were also invited.
- The workshop consisted of theoretical discussions in a classroom setting as well as field work to address topics involving capacity building, policy design and technical assistance for Central American countries. The workshop was consistent with the objectives of IICA's 2010-2014 Medium-term Plan approved by the Inter-American Board of Agriculture (IABA).

7.1.2. Objectives

7.1.2.1. General

- To raise awareness among members of Central America's biosafety commissions and delegates from the Andean Region of aspects of low level presence (LLP), and enhance their overall capacities so they may execute science-based risk assessments.

7.1.2.2. Specific objectives

- To facilitate the consolidation of a network among the participants.
- To share experiences in legal frameworks for biotechnology among the Central American and Andean regions, Canada, Mexico and the Dominican Republic.
- To promote capacity building for decision-making processes that involve genetically modified organisms (GMOs) and LLP.
- To share risk assessment manuals and guidelines.
- To introduce participants to novel genetically modified (GM) events (GM salmon in Panama and GM pineapple in Costa Rica).

7.1.3. Importance of the proposed event

The risk assessment course was important for the following reasons:
(*i*) It was one of the first technical activities of the ICABB;
(*ii*) It developed the technical capacities of (45) biosafety officials from 18 countries;
(*iii*) The presence of the UNEP-GEF made it possible for countries not members of IICA to take part (Cuba);
(*iv*) The event allowed the UNEP-GEF projects to interact, highlighting the need to support future regional initiatives on biosafety and environmental issues.
(*V*) It provided a unique opportunity to observe important regional GM events in the field;
(*vi*) The Andean Region officials who took part as observers witnessed the benefits of working as a region to address biosafety issues.

7.1.4. Outcomes

- Consolidation of the Central American Initiative on Biotechnology and Biosafety (ICABB)

- 42 officials (decision makers, national regulators and members of national biosafety committees) from 18 countries received training in biosafety risk assessment.

7.1.5. Methodology

A five-day workshop was held in Costa Rica from February 26 to March 2, 2013. The first three days were spent at IICA Headquarters and the last two at various sites near the Costa Rica-Panama border). For logistical reasons, the participants were in Costa Rica from February 25 to March 3.

The workshop followed methodologies developed by IICA and used successfully previous biotechnology and biosafety courses and workshops.

Given the importance of the event, the proceedings were edited, translated and published in an electronic format. IICA acted as the technical coordinator.

7.1.5.1 Official language

Spanish was the official language. However, simultaneous interpretation was provided.

7.2. Participants

Government regulators from the national biosafety authorities of the different countries.

(i) Guest speakers

Martin Lema (Argentina), Paulo Paes (Brazil), Luis Barnola (Ag-Canada), Phil Macdonald (CFIA, Canada), Alex May (Costa Rica), María Mercedes Roca (Honduras), Iveth Vargas (Panama), Luis Benavides (Panama), Ebrahim Firoozabady (USA), Marianela Araya (UNEP-GEF), and Pedro Rocha (IICA)

(ii) Participating countries

Argentina, Belize, Bolivia, Brazil, Canada, Colombia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, Dominican Republic, United States, and Venezuela.

Table 1. List of Workshop Participants (speakers, participants and authorities) February 25 - March 2, 2013

	Country	Name	Position	Institution	E-mail
	Speakers and participants				
1	Argentina	Martin Alfredo Lema	Biotechnology Director	Ministry of Agriculture and Livestock	mlema@minagri.gob.ar
2	Belize	Anil Kumar Sinha	Representative	CARDI	as012175@gmail.com
3	Belize	Caroline Mary Herron	Professor	University of Belize	cherron@ub.edu.bz
4	Belize	Eugene Waight	Chief Agriculture Officer	Ministry of Natural Resources & Agriculture	Eugene.waight@agriculture.gov.bz secretary@agriculture.gov.br
5	Belize	Francisco Adrian Gutiérrez	Technical Director, Plant Health Services	Belize Agricultural Health Authority	frankpest@yahoo.com
6	Bolivia	Cecilia Eugenia González Paredes	Professor of Biosafety Management	Ministry of the Environment and Water Resources	ceckiz@gmail.com
7	Brazil	Paulo Paes de Andrade	Speaker, Professor Genetics Department	Universidad Federal de Pernambuco	andrade@ufpe.br canoadetolda@gmail.com
8	Canada	Luis Guillermo Barnola	Speaker	AG CANADA	Luis.Barnola@agr.gc.ca
9	Canada	Philip Macdonald	Speaker	CFIA	Philip.Macdonald@inspection.gc.ca
10	Colombia	Gloria Patricia Cañas Gutiérrez	Technology Development and Health Protection Department	Ministry of Agriculture and Rural Development	gloria.canas@minagricultura.gov.co
11	Costa Rica	Alejandra Chaverri Soto	National Participant	Ministry of Health	achaverri@ministeriodesalud.go.cr
12	Costa Rica	Alejandro Hernández	Director of Science and Technology Promotion	Ministry of Science and Technology	alejandro.hernandez@micit.go.cr
13	Costa Rica	Alex May Montero	Director	National Biosafety Commission	alexmay@sfe.go.cr
14	Costa Rica	Esteban Cerdas Quirós	National Participant	Ministry of Health	ecerqui@gmail.com
15	Costa Rica	Giovanni Garro Monge	CTNBio Regulator and Coordinator of Biotechnology Research Center, ITCR	National Technical Biosafety Commission (CTNBio)	ggarro@itcr.ac.cr
16	Costa Rica	Jorge Arturo Madriz Muñoz	Project Manager UNEP-GEF	UNEP-GEF	madrizj@gmail.com
17	Costa Rica	Jorge Manrique Hernández Benavides	Coordinator, Wildlife Conservation and Management Program	National Technical Biosafety Commission (CTNBio)	jorgecrcr@yahoo.com
18	Costa Rica	Leda Madrigal Sandi	Head of Biotechnology Program, SFE	National Technical Biosafety Commission (CTNBio)	lmadrigal@sfe.go.cr
19	Costa Rica	Manuel Emilio Vargas Chavarría	National Participant	National Animal Health Service (SENASA)	mvargas@senasa.go.cr

20	Costa Rica	Marcela Jiménez Peralta	Assistant	State Plant Health Protection Department (SFE)	majimenez@sfe.go.cr
21	Costa Rica	Marianela Cascante Bejarano	Project Assistant UNEP-GEF	UNEP-GEF	mcascante@sfe.go.cr
22	Costa Rica	Pedro Rocha Salavarrieta	Coordinator, Area of Biotechnology and Biosafety	IICA Headquarters	Pedro.Rocha@iica.int
23	Costa Rica	Sylvie Braibant	National Participant	National Animal Health Service (SENASA)	sbraibant@gmail.com
24	Costa Rica	Walter Quiros	National Seed Office	National Technical Biosafety Commission (CTNBio),	wquiros@ofinase.go.c
25	Cuba	Leticia Pastor Chirino	Delegate	National Biological Safety Center	leticiach@orasen.co.cu
26	Cuba	Marvis Esther Suarez Romero	Delegate	National Biological Safety Center	marvis@orasen.co.cu
27	Ecuador	Segundo Angel Onofa Guayasamin	Biosafety Unit	Ministry of the Environment	anoafa@ambiente.gob.ec
28	El Salvador	Jeremias Ezequiel Yanes	Project Coordinator, "Safe Use of Biotechnology in El Salvador" Project	Ministry of the Environment and Natural Resources	jeremiasyanes@marn.gob.sv
29	Guatemala	Héctor Sagastume Mena	Researcher	Institute of Science and Agricultural Technology (ICTA)	hasagastume@yahoo.com biotecnologia.magoa@yahoo.com
30	Guatemala	José Mauricio Hernández de la Parra	Regulatory authority	DFRN-VISAR-MAGA	biotecnologia.maga@yahoo.com.
31	Honduras	Carlos Alberto Almendares Ordoñez	Chairman	CTN Bio Honduras	calmendares81@yahoo.com
32	Honduras	José Luis Matamoros Arrazola	Regulatory authority	CERTISEM/SENASA	josematamoros22@yahoo.com
33	Honduras	María Mercedes Doyle	Professor	Zamorano Agricultural University	mmroca@zamorano.edu
34	Mexico	Rocío Morales Martínez	Director of Industrial Sector Assessments	Secretariat of the Environment and Natural Resources	rocio.morales@semarnat.gob.mx
35	Nicaragua	Jorge Indalecio García Centeno	Regulatory authority	Ministry of Agriculture and Forestry	jorge.garcia@dgpsa.gob.ni
36	Panama	Judith Ivette Vargas Ascárraga	Chairman	Agricultural Biosafety Sectorial Committee (CSBA)	ivargas01@hotmail.com
37	Panama	Luis Manuel Benavides González	Head of Regulatory Department-AUPSA/Panama Biosafety Regulator	Panama Food Safety Authority (AUPSA)	lbenavides@aupsa.gob.pa
38	Panama	Marianela Araya	Program Officer	United Nations Environment Programme (UNEP)	marianela.araya@unep.org

39	Peru	Jorge Enrique Alcántara Delgado	Technical Coordinator	Regulation of the Agricultural Biotechnology Safety	jalcantara@inia.gob.pe
40	Dominican Rep.	Arsenio Heredia Severino		Dominican Agricultural and Forestry Research Institute (IDIAF)	megatoniv@hotmail.com
41	Dominican Rep.	Julio Bolívar Mejía Brea	Director of CEVIBE	Institute for Innovation in Biotechnology and Industry (IIBI)	mbreaj@yahoo.es
42	Dominican Rep.	Marina Alicia Hernández	Head of Genetic Resources Department	Ministry of the Environment and Natural Resources	Marina.Hernandez@ambiente.gob.do
43	USA	Cynthia Smith Palliser	Participant	USDA/FAS	smithpalliserc@state.gov
44	USA	Ebrahim Firoozabady	Speaker	Fresh del Monte	EFiroozabady@freshdelmonte.com
45	USA	Victor Gonzalez	Participant, Day 1	USDA/FAS	
46	Venezuela	Rodolfo Fernández Gómez	Researcher	Institute of Advanced Studies (IDEA)	rodfergom@gmail.com
	Special Guests				
47	Costa Rica	Ana Lorena Guevara	Vice-Minister	Ministry of the Environment, Energy and Telecommunications	vicemi@minae.go.cr
48	Costa Rica	Adolfo Ortiz Barboza	Vice-Minister	Ministry of Health	aortiz@ministeriodesalud.go.cr
49	Costa Rica	Keilor Rojas Jiménez	Vice-Minister	Ministry of Science and Technology	krojas@micit.go.cr
50	Costa Rica	Tania López Lee	Vice-Minister	Ministry of Agriculture and Livestock	tlopez@mag.go.cr
51	Costa Rica	Victor Villalobos	Director General	IICA Headquarters	Victor.Villalobos@iica.int
52	Costa Rica	Lloyd Day	Deputy Director	IICA Headquarters	Lloyd.Day@iica.int
	Translators				
53	Costa Rica	Luis Delgadillo	Interpreter	Language Arts S.A.	
54	Costa Rica	Thais Pardo	Interpreter	Language Arts S.A.	thaispardo@gmail.com
	Institutional Facilitators				
55	Costa Rica	Bryan Muñoz Castillo	Specialist	IICA Headquarters	Bryan.Munoz@iica.int
56	Costa Rica	Priscilla Segura		IICA Headquarters	Priscilla.Segura@iica.int
57	Costa Rica	Ronald Hidalgo		IICA Headquarters	Ronald.Hidalgo@iica.int
58	Costa Rica	Xinia Quirós Quesada	Specialist	IICA Headquarters	Xinia.Quiros@iica.int

7.3. Program

7.3.1. Summarized agenda

	Tuesday	Wednesday	Thursday	Friday	Saturday
Morning Block	Intro to risk assessment	Risk assessment for LLP/AP scenarios	Case study	Case Studies / Practical Instruction Field visit (GM salmon, Panama)	Case Studies / Practice Field visit (GM pineapple, Costa Rica)
Afternoon Block	Risk assessment for crops and forestry	Risk assessment for animals	Field Trip to Golfito		

7.3.2. Detailed agenda

Hour	Activity	Responsible
Day 1: Tuesday February 26, 2013 *Venue: IICA meeting, Coronado, Costa Rica*		
7:15 a.m.	Depart hotel	Priscilla Segura (IICA)
8:00 a.m.	Participant Registration	P. Segura (IICA)
8:15 a.m.	Welcome	L. Day (IICA) Representatives of Costa Rican Authorities (Min. Agriculture, Min Environment, Min. Health) J. Madriz (UNEP-GEF CR)
8:40 a.m.	Introduction	P. Rocha (IICA)
8:45 a.m.	Introduction of participants	Participants
9:00 a.m.	Basic information and techniques for risk assessment	Phil Macdonald (CFIA Canada)
10:00 a.m.	Coffee break	IICA
10:30 a.m.	Formulating problems and risk assessment	Marianela Araya (UNEP-GEF)
11:15 a.m.	Risk Assessment in agriculture: Experiences with GM maize in Honduras	María Mercedes Roca (CTNBio Honduras)
12:00 m.	Lunch	IICA
1:30 p.m.	Risk assessment in forestry	Paulo Paes (CTNBio Brazil)
2:15 p.m.	Case Study: Development of GM Pineapple - Experimental Basis	Ebrahim Firoozabady (USA)
3:00 p.m.	Workshop guidelines	Pedro Rocha (IICA)
3:05 p.m.	Coffee break	IICA
3:20 p.m.	Case Study Workshop: Basics of risk assessment in agriculture and forestry - Implications for environment, agriculture, health and economics.	All participants
4:40 p.m.	Conclusions	All participants
5:30 p.m.	Depart for hotel	IICA
Day 2: Wednesday February 27, 2013 *Venue: IICA meeting room, Coronado, Costa Rica*		
7:15 a.m.	Depart hotel	Priscilla Segura (IICA)
8:00 a.m.	Towards a Global Policy for Low Level Presence (LLP).	Luis Barnola (Ag-Canada)
9:00 a.m.	Argentina´s experience: Vision of an exporter country	Martin Lema (Argentina)
9:45 a.m.	Coffee break	IICA
10:15 a.m.	Costa Rica´s experience with LLP: Vision of an importing country.	Alex May (Costa Rica)
11:15 a.m.	Discussion panel: Economic impact of LLP policies and technical issues of risk assessment	All participants
12:00 m.	Lunch	IICA

1:30 p.m.	Regulatory issues involved in GM salmon	Judith Iveth Vargas (Panama)
2:15 p.m.	Regulatory issues involved in GM animals	Martin Lema (CTNBio Argentina)
3:00 p.m.	Workshop guidelines	Pedro Rocha (IICA)
3:05 p.m.	Coffee break	IICA
3:20 p.m.	Workshop: Risk assessment and GM animals (ethical, economic and environmental issues)	All participants
5:30 p.m.	End of session	
Day 3: Thursday February 28, 2013 *Venue: IICA meeting room, Coronado, Costa Rica*		
7:15 a.m.	Depart hotel	Priscilla Segura (IICA)
7:45 a.m.	Explanation of logistics- Field trip to Golfito	Pedro Rocha
8:00 a.m.	Basics of GM mosquitoes	Paulo Paes
8:45 a.m.	Case study: Regulatory issues involved in release of GM mosquitoes in Brazil and Panama	Paulo Paes Luis Benavides (Panama)
9:45 a.m.	Coffee Break	IICA
10:15 a.m.	Biotechnology 2012: Maize, cancer and rats	Pedro Rocha
10:30 a.m.	Discussion panel: Scientific rigor and GMO	All participants
11:30 m.	Lunch	IICA
12:20 p.m.	Depart for Golfito (by bus)	IICA/UNEP-GEF Costa Rica
3:30 p.m.	Scheduled stop	
3:50 p.m.	Continue trip to Golfito	
7:00 p.m.	Arrival in Golfito - Hotel Sierra http://www.hotelsierra.com	
Day 4: Friday March 1, 2013 *Venue: Golfito-Buenos Aires*		
6:00 a.m.	Depart for Volcan (Panama)	IICA/UNEP-GEF Costa Rica
6:45 a.m.	Arrival at Panama immigration checkpoint	
7:00 a.m.	Costa Rica immigration checkpoint	
8:30 a.m.*	Panama immigration checkpoint	
10:00 a.m.*	Coffee break	
11:30 a.m.*	Continue field trip to Volcan	
12:15 p.m.*	Arrival at Volcan	
12:15 p.m.*	Lunch	
1:00 p.m.*	Visit GM salmon ponds	
3:00 p.m.*	Depart for Costa Rica	
3:45 p.m.*	Arrival at Panama immigration checkpoint	
4:00 p.m.*	Panama immigration checkpoint	
5:00 p.m.	Costa Rica immigration checkpoint	
5:30 p.m.	Arrival at Hotel Sierra (Golfito, Costa Rica)	
Day 5: Saturday March 2, 2013 *Venue Golfito-Buenos Aires*		
7:00 a.m.	Depart Golfito for Buenos Aires, Costa Rica	IICA/UNEP-GEF Costa Rica
10:30 a.m.	Arrival and field visit- GM pineapple cultivars	
12:00 a.m.	Lunch	
6:00 p.m.	Arrival San Jose	

* Panama time

Annexes

Annex 1. List of useful database access links for biosafety analysis

Biosafety Clearing House: http://bch.cdb.int

UNEP-GEF Biosafety website – www.unep.org/biosafety with links on projects, publications, toolkits, case studies and lessons learnt

Developed Biosafety Clearing House training materials - http://bch.cbd.int/help/topics/en/webframe.html?Training_Materials.html

UNEP-GEF Biosafety Media channel (YouTube) – beta version (developed in last quarter of 2011) - http://www.youtube.com/user/UNEPBIOSAFETY?feature=watch

ICGEB main website: http://www.icgeb.org

ICGEB Problem formulation article:
http://www.icgeb.org/~bsafesrv/pdffiles/Col6_Gray.pdf
http://www.icgeb.org/~bsafesrv/ : link to ICGEB databases.

Annex 2.

International Statement on Low Level Presence

1. The United Nations Food and Agriculture Organization recently indicated that global agricultural production would need to increase by 70 percent by 2050 in order to meet the rising international food demand. However, significant constraints, such as limited access to arable land and fresh water will affect countries' ability to increase production. Given this reality, the increase in agriculture production would need to come from an increase in productivity. To this regard, biotechnology is going to play a critical role.

2. In addition to helping address food security challenges, biotechnology would assist in mitigating climate change impacts by, for example, supporting agricultural practices that could improve sustainable and efficient agriculture.

3. Today, the number and complexity of genetically engineered crops being developed and cultivated worldwide is increasing annually. This situation threatens to increase the number of asynchronous and asymmetric approvals worldwide and, consequently, increase the risk of trade disruptions resulting from the low level presence (LLP) of unapproved events in commercial channels. Reducing asynchronous approvals is the most effective way of reducing trade disruptions due to LLP. However, there is an immediate need to address the risk to trade arising from LLP occurrences, a risk that impacts importer and exporting countries alike, and global food security in general.

4. Recognizing the need for action, we, importer and exporting countries, have decided to discuss the issue of LLP; exchange information on its origin and potential implications on the agricultural trading system; and begin the development of an approach or set of approaches to manage LLP internationally.

5. We recognize the importance of developing practical approaches for the management of LLP that are science-based, predictable and transparent, and that will encourage the use of international science-based guidelines on LLP, such as Annex 3 of the *Codex Alimentarius*: Food Safety Assessment in Situations of Low-Level Presence of Recombinant-DNA Plant Material in Food.

6. We recognize that the approaches could be implemented on a voluntary basis by countries.

Therefore, we, importer and exporter countries have decided to:

7. *Work* collaboratively on the issue of LLP to facilitate international trade of agriculture commodities by developing practical approaches, designed to address LLP globally;

8. *Define*, for the purpose of this initiative, LLP for food as low levels of recombinant DNA plant materials that have passed a food safety assessment according to the *Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* (CAC/GL 45-2003) in one or more countries, but may on occasion be present in food in importer countries in which the food safety of the relevant recombinant-DNA plants has not been determined;

9. *Work* to ensure that the approaches include both food and feed;

10. *Continue* to work collaboratively to address the overarching problem of asynchronous approvals, while working to mitigate the impact of LLP situations;

11. *Work* collaboratively to address the risk of trade disruptions resulting from LLP in order to facilitate international trade of agriculture commodities by developing an approach or approaches, designed to facilitate the management of LLP globally;

12. *Recognize* that LLP of unapproved seed in commercial channels is also a challenge to seed trade and that it also requires collaborative efforts to address. Further collaborative efforts on seed through this initiative should be informed by the work being currently undertaken by the Organization for Economic Cooperation and Development (OECD) in this area;

13. *Assure* that these practical approaches do not compromise human, animal, and plant health and safety;

14. *Facilitate* the timely and continued exchange of information on domestic policies related to LLP; and

15. *Continue* to implement the International Work plan on Low Level Presence which structures our collaborative actions leading to the development of practical approaches to reduce international trade risks related to LLP, with a view to have Ministers considering the endorsement of an approach or a set of approaches designed to facilitate the global management of LLP.

Vancouver, Canada, 22nd of March 2012

Annex
List of countries subscribing the International Statement on Low Level Presence

Australia
Argentina
Brazil
Canada
Chile
Costa Rica
Mexico
Paraguay
Philippines
Russia
United States
Uruguay
Vietnam

Last update: August 31, 2012

Annex 3. Program for signature of ICABB constitution agreement and its first official meeting.

Hour	Activity	Responsible
Day 1: Monday 25th February 2013 *Place: Argentina´s room, IICA, Costa Rica* *Participants: Presidents or Representatives of the National Commissions of Biosafety of Belize, Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, Nicaragua and Panama.*		
7:15 a.m.	Depart hotel	Priscilla Segura (IICA)
8:00 a.m.	Registration	P. Segura (IICA)
8:20 a.m.	Words of Welcome	Victor Villalobos (IICA) Lorena Guevara (MINAET)
8:45 a.m.	"Central American Initiative on Biotechnology and Biosafety" – ICABB: Joint Construction of an Opportunity for Technical Integration"	Pedro Rocha (IICA)
9:15 a.m.	Signing of the document	Representatives of the countries
9:30 a.m.	Coffee break	IICA
10:00 a.m.	Designation of General Coordinator and Secretariat Approval of general procedures for the meeting Definition of priorities and start of work plan	Delegates
12:00 m.	Lunch	IICA
1:00 p.m.	Discuss work plan	Representatives of the countries General Coordinator Secretariat
3:00 p.m.	Coffee break	IICA
3:15 p.m.	Discussion of work plan	Representatives of the countries General Coordinator Secretariat
5:00 p.m.	End of session	General Coordinator

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