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AD HOC TECHNICAL EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT UNDER THE CARTAGENA PROTOCOL ON BIOSAFETY
First meeting
Montreal, 20-24 April 2009

TRANSCRIPT OF THE DISCUSSION GROUPS UNDER THE OPEN-ENDED ONLINE EXPERT FORUM ON RISK ASSESSMENT AND RISK MANAGEMENT

Note by the Executive Secretary

1. At its fourth meeting, the Conference of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP), in its decision BS-IV/11, established an Open-ended Online Expert Forum on Risk Assessment and Risk Management through the Biosafety Clearing House (BCH). In the same decision, the Parties also established an Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management.

2. The Executive Secretary was requested to convene, prior to the fifth meeting of the Conference of the Parties serving as the meeting of the Parties to the Protocol, to be held in October 2010: (i) ad hoc online discussion groups; (ii) two AHTEG meetings; and (iii) at least one real-time online conference per region prior to each of the two AHTEG meetings.

3. In order to implement decision BS-IV/11, the Secretariat, with the approval of the Bureau of the Conference of the Parties serving as the meeting of the Parties to the Protocol, launched a continuous process comprising the following events:

(a) An open-ended online forum;

(b) Discussion groups on specific topics;

(c) Two series of regional real-time online conferences (one prior to each AHTEG meeting); and

(d) Two AHTEG meetings.

4. The objective of the discussion groups was to identify major issues related to specific aspects of risk assessment and risk management. A total of eight topics of discussion were chosen on the basis of recommendations made during previous risk assessment workshops. 1/ These topics were:

1/ UNEP/CBD/BS/COP-MOP/4/INF/13 –17.

(a) Risk assessment and risk management of transgenic fish;

(b) Risk assessment and risk management of transgenic trees;

(c) Risk assessment and risk management of transgenic microorganisms and viruses;

(d) Risk assessment and risk management of transgenic pharmaplants;

(e) Risk assessment and risk management of LMOs with stacked genes or traits;

(f) Post-release monitoring and long-term effects of LMOs released into the environment;

(g) Risk assessment and risk management of specific receiving environments; and

(h) Flowchart ("roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol.

5. The discussion groups were organized in two rounds of four simultaneous topics, and discussions were open for three weeks on each topic during the period from 10 November to 19 December 2008. By the launching of the discussion groups, a total of 147 national experts from 48 countries and 36 observers had been registered to the online forum. Eighty-eight interventions were posted in the eight discussion groups.

6. The full transcript of the discussion groups is contained in the annex to this document.

7. A synthesis document containing an analysis of the open-ended online expert forum on risk assessment and risk management has been prepared by the Secretariat for submission to the Ad Hoc Technical Expert Group. 2/

2/ UNEP/CBD/BS/AHTEG-RA&RM/1/2.

Annex

FULL TRANSCRIPT OF THE DISCUSSION GROUPS OF THE OPEN-ENDED ONLINE EXPERT FORUM ON RISK ASSESSMENT AND RISK MANAGEMENT UNDER THE CARTAGENA PROTOCOL ON BIOSAFETY

List of topics:

1. Risk assessment and risk management of transgenic fish.
2. Risk assessment and risk management of transgenic trees.
3. Risk assessment and risk management of transgenic microorganisms and viruses.
4. Risk assessment and risk management of transgenic pharmaplants.
5. Risk assessment and risk management of LMOs with stacked genes or traits.
6. Post-release monitoring and long-term effects of LMOs released into the environment.
7. Risk assessment and risk management of specific receiving environments.
8. Flowchart ("Roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol.

TOPIC 1 - RISK ASSESSMENT AND RISK MANAGEMENT OF TRANSGENIC FISH

Introduction to the topic

by Anne R. Kapuscinski and Kelly M. Pennington, University of Minnesota, St. Paul, MN 55108, USA. E-mail: kapus001@umn.edu

Research and development of genetically modified or transgenic fish is underway for intended uses in aquaculture. There is a need for systematic and broadly accepted methodologies to assess and manage environmental risks of this biotechnology. There is very little experience in environmental risk assessment of transgenic fish using case-specific and ecologically relevant data. Methodologies do exist for this task but have not been fully utilized. To address this need, a team of 40 co-authors from 19 countries wrote a peer-reviewed book, *Environmental Risk Assessment of Genetically Modified Organisms: Methodologies for Transgenic Fish* (see the Selected Readings page and note by the author below). This book synthesizes the best science-based methodologies that countries can apply to conduct their own ecological risk assessments and develop risk management measures for proposed uses of transgenic fish on a case-by-case basis. The authors discuss the flexibility, utility, and limitations of these methodologies. The methodologies are also relevant to transgenic crustaceans and molluscs, as well as to aquaculture lines produced by traditional selective breeding.

Any risk assessment process based on scientific analysis should be linked with transparent involvement of relevant stakeholders at key points. This "analytic-deliberative" process recognizes the need for both high-quality science and the input of affected parties. One particular method for involving stakeholders is Problem Formulation and Options Assessment (PFOA), a process for science-guided multi-stakeholder involvement in environmental risk assessment in which stakeholders identify what societal need may be addressed by the transgenic fish, consider other technology options, deliberate on benefits and risks of the identified options and develop recommendations for decision makers.

Potential environmental hazards associated with escape or intentional release of a specific line of transgenic fish range from changes occurring at the molecular level to the ecosystem level. Therefore, methodologies from molecular biology, population genetics, ecology, and other scientific fields all must be applied to risk assessment of transgenic fish. A complete environmental risk assessment estimates the

probability and magnitude of gene flow from transgenic to wild relatives; and the probability, magnitude and severity of ecological effects, with or without gene flow. To understand whether or not a specific environmental harm will occur, care must be taken to identify traits of the fish and components of the ecosystem which are feasible to measure and are reliable indicators of the ecological change that is of concern. Risk assessments need to openly treat the uncertainty that exists at each step in the environmental risk assessment process, by using uncertainty analysis methods from a range of available qualitative and quantitative tools.

Risk management of transgenic fish is currently focused on two methodologies: physical and biological confinement of fish to minimize their entry into and spread in nature; and monitoring to detect presence, establishment and ecological effects of escaped or intentionally released fish. Risk management practices should be based on conclusions from a risk assessment and not replace the need to conduct a science-based and transparent risk assessment.

Gaps remain in human and institutional capacity needed to conduct science-based and socially robust risk assessments of transgenic fish. Large gaps exist in data for assessing effects on specific ecosystems. Major needs are to: (a) fill key gaps in baseline ecological data on aquatic ecosystems and improve access to databases; (b) establish confined facilities with semi-natural conditions for conducting risk assessment tests, ideally as international cooperative research facilities in different ecological regions; (c) fill major gaps in public data on ecologically relevant traits of transgenic fish lines, especially for those closer to seeking commercial approval; and (d) develop in-depth risk assessment training programs for key participants in the process of risk assessment of transgenic fish and other genetically improved lines. Human capacity building should target aquatic scientists, from molecular biologists to community ecologists, who produce research data that can inform government-mandated risk assessments or who conduct the risk assessments; as well as regulatory affairs and biotechnology staff in public and private sector organizations which inform the ultimate decision-makers.

Note by the author: Courtesy copies of this cited book were distributed to developing-country scientific libraries and various entities involved with aquaculture and fisheries. A very small number of courtesy copies remain. To request a copy, write an email message that confirms you are from a developing country, gives your current job title and full work address, and explains why you need this book; and send to isees@umn.edu, with subject line "book request to Anne Kapuscinski".

Suggested points for discussion

- How to apply Annex III when assessing the risks of transgenic fish;
- Experience in conducting risk assessment of transgenic fish;
- Difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc.;
- Elements necessary to conduct risk assessments of transgenic fish;
- Issues that are unique to this topic;
- Recommendations for preparing risk assessment reports.

List of threads and number of replies

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Interventions

A. Welcome [#740] - posted on 2008-11-09 22:00 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Risk assessment and risk management of transgenic fish".

The discussions within this group will take place during 10-23 November 2008.

To assist in the discussions, a non-exhaustive list of suggested reading materials, as well as an introduction to the topic, have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum has been made available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

As a participant to the Open-ended Online Expert Forum on Risk Assessment and Risk Management, your contribution is of extreme importance in making this Forum an unprecedented medium of discussion which is a forerunner to the intergovernmental negotiations on the development of guidance material on specific aspects of risk assessment of LMOs.

The CBD Secretariat thanks you for your active participation. Happy discussions!

Best regards,

The Biosafety Division

Reply to #740: Welcome [#809] - posted on 2008-11-27 16:35 by Dr Marja Ruohonen-Lehto

Thank you. I have followed the discussions and will provide input before closure date. Due to travelling I am only joining now.

Marja Ruohonen-Lehto

B. Transgenic fish - some comments to the on-line discussions [#836] - posted on 2008-11-30 11:35 by Dr Marja Ruohonen-Lehto

My name is Marja Ruohonen-Lehto and I work at the Finnish Environment Institute in Helsinki, Finland. I give expert advice on biosafety issues and environmental risk assessment (ERA) of GMOs. I am not a specialist in fish but I have followed the field for about 10 years. I am together with colleagues from the

US and Norway co-leading the writing of an OECD consensus document on Atlantic Salmon. Moreover, I chaired the fish working group in the Canada-Norway expert workshop on risk assessment for emerging applications of LMOs in Montreal, June 2007.

The working group identified some recommendations: on method development needs (e.g. for collecting basic biological data, including ecological niches and local genotypes, for baseline data, for identification of critical life stages and critical environmental variables and fitness components); on development of different worldwide scenarios on the introduction of transgenic fish into the environment; on performing sensitivity analysis in models to identify parameters for which we still lack experimental data; on identifying other likely candidate model fish to be used in case studies for ERA; and last but not least to develop case-by-case protocols for transgenic fish risk assessment.

I would especially like to thank the comments provided to this discussion where it was clearly stated that we still lack data on basic biology, physiology and ecology of many of the fish species.

I would like to finish by drawing your attention to some resent work carried out by Kata-Riina Valosaari, Sami Aikio and Veijo Kaitala on mating preference and strategy in growth enhanced fish. The work is published in Oikos in 2008 and in Evolutionary Applications either late 2008 or early 2009.

C. How to apply Annex III when assessing the risks of transgenic fish [#786] - posted on 2008-11-21 17:57 by Leticia Pastor Chirino

Please, I would like to express Cuba´s opinion in relation to the topic How to apply Annex III when assessing the risks of transgenic fish. In the case of Cuba at this moment only one research involving transgenic fish development has been authorized, this research is still in an early stage, with a small number of fish under confinement conditions. The Annex III of the Protocol in Cuba began through Resolution 180/2007: ¨Regulation for the Authorization License of Biosafety¨, that counts on a general part and a group of annexes and of them 3 are referred to activities related with transgenic fish, this annexes are a guide to the preparation of the technical reports to ask for authorization, information that is the base for the realization of risk assessment and afterwards the decision making. In our case, the process of decision making generally is the same, and the differences are in the information to be presented in relation with the organisms in discussion and the activity to be carried out and elements that define the experts to be consulted and the controlled methods to be used. In Cuba we count on a technical instrument used as a guide called ¨LIVING MODIFIED ORGANISMS, A GUIDE FOR RISK AND MANAGEMENT ASSESSMENT¨ by the regulation organ for the risk assessment in which is define within other elements the steps to be taken and describes possible qualitative techniques to be used.

Leticia Pastor

National Centre for Biosafety, Cuba

D. Risk Assessment for Transgenic Fish [#777] - posted on 2008-11-20 16:13 by Dr. Ronald Stotish

Risk assessments are performed every day in a variety of private and public organizations. The methodology has improved with experience, and the development of tools to perform better assessments of possible risks, and the adequacy of proposed risk mitigation. The suggestion that risk assessment should include subjective assessment of social, cultural, or economic needs for new technology troubles me greatly, because there are no clear unambiguous standards upon which to base such an assessment, and reasonable people undoubtedly differ greatly in their perspective and value basis for reaching those

decisions. Furthermore, if we accept there are data gaps in our ability to anticipate unforeseen consequences, we should apply the same uncertainty to any consideration of "value" of a new technology.

Secondly, to suggest we cannot address risk of transgenic fish without filling our human capacity and data gaps presumes we know how to fill those gaps, and have the resources to do so. I would posit we can approach these issues on a case by case basis, and evaluate the risk a particular application may represent on its merits, and on the merits of the proposed risk mitigation steps proposed by its sponsor. The effectiveness of those steps should be measurable, and there must be consequences if subsequent experience demonstrates the risk assessment was flawed. I believe to do otherwise unfairly constrains the sponsor to addressing a hypothetical case, for which there is no definable endpoint.

Lastly, I believe our national and international bodies have the capacity to perform thoughtful and meaningful risk assessments, and to evaluate new technologies objectively, solely on their merits. Suggestions of a multi-stakeholder public process merit consideration, and there are certainly opportunities to involve experts to improve the process. In my view, however there is a responsibility to assure the process does not deteriorate into a subjective, and non-productive, debate involving attitudes that are outside the precise confines of an objective consideration of the issues. There are many examples of issues in our daily lives where well meaning people disagree for moral, religious, or political reasons. They are entitled to their beliefs, and to the personal choices derived from their beliefs. However, I believe to unfairly restrict new technologies based on minority views would be a failure of our responsibility to the remainder of our global society.

E. Guidance on risk assessment for Transgenic fish [#761] - posted on 2008-11-16 11:22 by Dr Ossama Abdel-kawy

Several governments have addressed the issue of research on fish, but many have not addressed transgenic fish directly. The U.S.D.A. developed guidelines (standards) for research on genetically modified fish and shellfish (US ABRAC 1995). In Europe, legislation and guidance is addressed in Directive 2001/18/EC which is implemented by Member States. An example is the U.K Statutory Instrument 2002 #2443 (2002) on release of GM animals. The UK Advisory Committee on Release to the Environment (ACRE) also issued a guidance note on releases to the environment of transgenic fish. In the Canadian regulatory system the Canadian Environmental Protection Act addresses regulation of any animal that is not contained, including transgenic fish. In general the approach to risk management has been through containment.

Mechanisms employed to prevent potential adverse effects to the environment include mechanical containment systems and/or biocontainment such as those reviewed in Devlin and Donaldson 1992. Closed water systems have been used in research on transgenic fish to ensure no escape into the environment as utilized by Rahman et al (2001). The most commonly used biocontainment method is through heat or pressure shock sterilization for induction of triploidy (Benfey 1999). Induction of triploidy is not 100% effective, nor is it commercially feasible for all species. Triploidy also has effects on the reducing fish growth (Devlin et al 2004). Transgenic sterilization is also a potential mechanism. (Dunham 2004, MacLean et al 2002)).

Potential environmental risks of living modified fish species has been addressed in several recent reviews (Devlin et al. 2006; MacLean et al, Biosafety Reviews 2: 36-65 2005, Muir and Howard, Transgenic Research 11: 101-114 2002), USDA, ABRAC Performance standards for genetically modified fish, 1995), (Royal Society UK, The use of GM organisms, May 2001), (US Congressional Research Services July 2005 Genetically engineered Fish and seafood., U.S. National Research Council 2004 Animal Biotechnology Science Based Concerns, National Academies Press). The US NRC indicates that transgenic fish pose the “greatest science based concerns associated with animal biotechnology in large

part due to the uncertainty inherent in conducting predictive risk assessments and the difficulty of remediation".

Reply to #761: Guidance on risk assessment for Transgenic fish [#769] - posted on 2008-11-17 18:08 by Kelly M Pennington

Most recently (September 18, 2008) the US Food and Drug Administration (FDA) released a draft guidance document for genetically engineered animals (available here: http://www.fda.gov/cvm/GEAnimals.htm).

F. Comments on assessing the risks on Transgenic fish [#753] - posted on 2008-11-13 22:58 by Mr Pisey Oum

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1. I think to apply Annex III t the Protocol, Parties should develop their own risk assessment guideline to adjust to their domestic or regional legal framework. Then the risk assessment framework should address the issue of non-safety, international agreements, stakeholder input, public opinion, national policies and the risk assessment of itself. The risk assessment of transgenic fish should include hazardous to ecosystem before the release, toxicity to non-target organisms, allergenicity to humans, gene transfer within fish, level of invasiveness, etc.

2. We don't have experiences in assessing risks from transgenic fish because there is no transgenic fish import yet into the country.

3. Prior required information on the transgenic fish is important from the applicants. Any assessed result on the fish should be requested from to the applicants or the country of export (party of export) including receiving environment, environmental interaction, parental organisms and recipient.

4. Recommendations for preparing risk assessment report:

- introduction,
- regulation of LMOs fish
- application
- application evaluation process
- hazard identification
- risk assessment
- risk evaluation
- conclusion of risk assessment
- summary of risk assessment
- reference.

Pisey Oum

Cambodia's Ministry of Environment

Reply to #753: Comments on assessing the risks on Transgenic fish [#767] - posted on 2008-11-17 14:30 by Dr Eliana Fontes

My name is Eliana Fontes and I was indicated by the Brazilian government to participate in this forum. I am not a fish specialist, so I am going to ask a general question to the forum participants to bring to the discussion some issues that are relevant to the risk assessment of GM fish. They are simple question that might seem irrelevant, but in my view they are basic background to follow the debates on the points for discussion suggested by the secretariat.

The risk assessment of GM crops currently in the market took in great part into consideration the concept of familiarity with the crop species in which the new genes have been inserted, and in the fact that most or all of the transformed crop varieties are the result of decades of conventional breeding and usually highly dependent on human intervention to survive and reproduce. It is thus expected that such varieties would have lower chance to compete and survive in the wild, in case of escape. My question to the fish specialists is: what is the degree of familiarity that we have with the fish species that are being subject of genetically engineering research? How much do we know about their genetics, have they been conventionally bread and further released into the environment? If so, has the impact of improved individuals in the introduced environment been measured? Has non-transgenic individuals of these species been introduced into new environments and if so, what has been the impact of such introduction, particularly to the local food chain?

This is a reply to 767 RE: Comments on assessing the risks on Transgenic fish [#768] - posted on 2008-11-17 17:54 by Kelly M Pennington

Dear Dr. Fontes and other forum participants,

I am a Ph.D. Candidate studying gene flow from genetically engineered fish to unmodified (wild-type) conspecifics. I'm using growth-enhanced Japanese medaka (*Oryzias latipes*) as a model species for the gene flow experiments that I'm doing in a confined laboratory environment.

Dr. Fontes asked some excellent questions - I'll answer them to the best of my knowledge, and encourage others to reply to this post with more information where available.

"- what is the degree of familiarity that we have with the fish species that are being subject of genetically engineering research?"

Some of the fish species nearest to commercialization as transgenic varieties include Common carp, tilapia, Atlantic salmon, and mud loach (Table 3.1 in the book, Environmental Risk Assessment of Genetically Modified Organisms. Volume 3: Methodologies for Transgenic Fish, 2007, by A. R. Kapuscinski et al. (editors) - see the list of Selected Readings for this discussion group). The degree of familiarity with these fish depends on the species: for mud loach and tilapia there are gaps in our knowledge even about basic biology and physiology, and for most fish species we don't know much about their ecology. In almost all cases, these fish species are less well-known to us than the crop plants that have been genetically modified.

"How much do we know about their genetics, have they been conventionally bread and further released into the environment? If so, has the impact of improved individuals in the introduced environment been measured?"

Compared to the highly domesticated crop plants Dr. Fontes referred to, we know relatively little about the genetics of most commercially important fish species - in fact, there may be no example of a truly "domesticated" fish line. Many farmed fish species have been subject to selective breeding to maximize particular traits (catfish, salmon, rainbow trout); one of the few tropical fish that has been part of a formal breeding program is the GIFT tilapia. Other farmed fish are not part of an intentional breeding program but may be under different selection pressures because they are reared in a farm environment, resulting in a genotype different from that of wild conspecifics. Very little is known about the impacts of escaped farmed fish - except that escaped/introduced fish exist outside their natural ranges. Tilapia, for example, have been intentionally introduced and have escaped from farms throughout the tropics. However, *measurements* of the environmental impacts of these fish in the wild are lacking.

"Has non-transgenic individuals of these species been introduced into new environments and if so, what has been the impact of such introduction, particularly to the local food chain?"

Much of the work on escaped farmed fish has been with Atlantic salmon, and a lot of that research has focused on impacts mediated by reproduction and interactions with wild populations (i.e., McGinnity, P. et al. "Fitness reduction and potential extinction of wild populations of Atlantic salmon, Salmo salar, as a result of interactions with escaped farm salmon" Proc. R. Soc. Lond. B (2003) 270, 2443–2450; Fleming, I. et al. "Lifetime success and interactions of farm salmon invading a native population" Proc. R. Soc. Land. B (2000) 267, 1517-1523). Measurement of a specific environmental impact like the effect on the local food chain is very challenging. If other forum participants are familiar with research investigating local food chain impacts of introduced/escaped fish, please reply to this post.

Overall, Dr. Fontes's questions seem to bring us back to discussion points #3 ("Difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc.") and #4 ("Elements necessary to conduct risk assessments of transgenic fish"). In many cases we are hampered by a lack of baseline data that could help us assess the ecological impacts of transgenic fish. Figure 6.1 in Devlin et al. (2007), "Assessing Ecological Effects Prior to Entry into Nature" (Chapter 6 of the book Environmental Risk Assessment of Genetically Modified Organisms. Volume 3: Methodologies for Transgenic Fish), presents one series of questions to ask to guide the process of assessing ecological effects of transgenic fish:

1. What are the relevant ecosystem components and processes?
2. What are the relevant phenotypic characteristics of the transgenic fish?
3. What are the most important interactions between the ecosystem components and the transgenic fish's phenotype?
4. What is the likelihood that genotype-environment interactions will affect the transgenic fish's phenotype in the environment of interest?
5. What unexpected environmental responses might result?
6. What are the consequences of the identified ecological effects, and how likely are they?

These questions could also be applied to better understanding the ecological impacts of selectively bred lines of fish.

While the answers to these questions are still not simple, they do provide a framework for collecting some of the data needed to understand potential ecological effects of a given transgenic fish.

G. Risk Assessment and Risk Management of Transgenic Fish [#754] - posted on 2008-11-14 04:03 by Mr. Rufus Ebegba

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The risk assessment of transgenic fish is to deal with the uncertainties associated with it in order that decisions may be made in full consideration of potential consequences in handling ,transfer and the use of it, both to the environment and human health .

The risk assessment of transgenic fish should be centred on the following considerations:

- Toxicity
- Allergenicity
- The genetic construct
- Impact on other organisms in the environment, fish inclusive .

For effective management of transgenic fish ,there should be phynotipic maker gene transferred in it, for easy of identification and withdrawal from the environment in the event there are identified later adverse effects associated with the transgenic fish.

TOPIC 2 - RISK ASSESSMENT AND RISK MANAGEMENT OF TRANSGENIC TREES.

Introduction to the topic

by Dr. Sofía Valenzuela A., Biotechnology Center and Forest Science Faculty, Universidad de Concepción, Concepcion, Chile. E-mail: sofvalen@udec.cl

The high demand of wood for industrial, heating, structural wood and fuel will require that in a short term time the area of forest plantations should be increased. In comparison to agricultural crops, trees planted for wood production are still undomesticated plants, having an enormous genetic potential that could be expressed in valuable new varieties. Biotechnology has been used as a tool for improving trees in the last years, the first genetically modified (GM) tree being developed in 1988. Traits under study for the development of GM trees include improving wood quality (lignin and cellulose amounts), flowering control, disease resistance and stress tolerance. In fruit trees, the main traits under study include virus resistance and fruit quality.

Some specific characteristics of trees include: large population size, many years before flowering, complex ecological backgrounds, low domestication, perennials, wind pollinated. These issues raise concerns regarding the introduction of GM trees into the environment, especially with traits which can give a better fitness, as high-growth. At a commercial level, two cases of environmental release of GM trees have occurred, GM papaya in Hawaii in 1997 and GM poplar in China in 2002 have been reported.

To date, no risk assessment (RA) studies which predict with any certainty the impact of releasing GM trees on native biodiversity has been reported. The main issue that has been discussed is gene flow, but little research has been done on the impacts that the transgene(s) might have on fitness or other ecological characteristics. Knowledge of gene flow in forest trees is still unsatisfactory due to continued shortcomings of available markers, inherent limitations of statistical models. Ecological risks from non-native species and their spread is known to be unpredictable, and if it occurs can have very significant effects. A sufficient number of field studies in diverse environments need to be conducted to determine if the physiological and fitness modifications are significant or not. These field trials need to be conducted for several years and in environments (sites), since there is a strong genotype x environment effect on trees that can affect fitness.

Currently, there are several GM-tree species that are herbicide tolerant and or have been transformed using marker genes, which have already been tested at field trials. The development of GM trees has increased in the last years, having more than 200 field trials involving at least 15 forest species. However, traits with large economical value in forestry as stress tolerance, low lignin and high cellulose levels and others will require the introduction (or suppression) of many genes. Therefore transformation will include the introduction of several genes, in order to obtain the trait of interest.

Since trees are long-lived, often producing copious amounts of pollen and seeds and in some cases they multiply asexually. Some aspects of risk management of GM trees that call for further consideration include the following: 1. Flowering control: sterility is one way of controlling the spread of transgenic trees to surrounding populations of related trees. In some species, however, more seed or fruit production might be desired, such as those with high wildlife value. Flowering control is, thus, a higher priority research item than is sterility. 2. Isolation of transgenic populations: establishment of transgenic plants in an environment far away from their relatives in order to avoid introgression of modified plants with indigenous populations. 3. Establish refugia or connecting corridors of stands of non-transformed trees when designing plantations. This strategy is a combination of factors associated with the maintenance of unaltered populations of trees in the midst of plantations that have been engineered for selected morphological and physiological properties.

Despite the differences between agricultural crops and trees, the general principles and methodologies for risk assessment as described in Annex III of the Cartagena Protocol can also be applied to GM-trees. The

framework for RA can be used to address specific issues raised by trees. The biosafety issues associated with transgenic trees will require that in-depth analysis is carried out on specific traits.

References provided by the author

- Balocchi C, Valenzuela S (2004) Introduction to GMOs and Biosafety in Forestry. In: Kellison R, MCcord S, Gartland K (eds.) Proceedings of the Forestry Biotechnology Workshop, Global Biotechnological Forum, 2-5 March 2004, Concepción, Chile, p. 85-96. (reprint)
- Burley J (2001) Genetics in sustainable forestry: the challenges for forest genetics and tree breeding in the new millennium. Canadian J For Res 31: 561-565. (abstract)
- Fenning T, Gershenzon J (2002) Where will the wood come from? Plantation forests and the role of biotechnology. Trends Biotech Sci 20: 291-296. (abstract)
- Kellison R, Balocchi C, Valenzuela S, Rodríguez J (2007) Forest biotechnology: An extension of tree improvement. Intl J Biotech 9: 448-459. (abstract)
- Kikuchi A, Watanabe K, Tanaka Y, Kamada H (2008) Recent progress on environmental biosafety assessment of genetically modified trees and floricultural plants in Japan. Plant Biotech 25: 9-15. (reprint)
- Peña L, Seguin A (2001) Recent advances in the genetic transformation of trees. Trends in Biotechnology 19: 500-506. (abstract)
- Snow A, Andow DA, Gepts P (2005) Genetically engineered organisms and the environment: Current status and recommendations. Ecol App 15: 377-404. (reprint)
- Strauss S, Brunner A, Busov V, Ma C, Meilan R (2004) Ten lessons from 15 years of transgenic Populus research. Forestry 77: 455-463. (abstract)
- Valenzuela S, Strauss S (2005) Lost in the woods. Nature Biotech 23: 532-533. (reprint)
- Valenzuela S, Rodríguez J, Balocchi C (2006) Transgenic trees and forestry biosafety. Elect J Biotech 9: 335-339. (reprint)
- Wolfenbarger LL, Phifer PR (2000) The ecological risks and benefits of genetically engineered plants. Science 290 : 2088-2093. (reprint)

Suggested points for discussion

- How to apply Annex III when assessing the risks of transgenic trees;
- Experience in conducting risk assessment of transgenic trees;
- Difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc.;
- Elements necessary to conduct risk assessments of transgenic trees;
- Issues that are unique to this topic;
- Recommendations for preparing risk assessment reports.

List of threads and number of replies

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H. Guidance on risk assessment for Genetically modified trees 0

Interventions

A. Welcome [#741] – posted on 2008-11-09 22:03 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Risk assessment and risk management of transgenic trees".

The discussions within this group will take place during 10-23 November 2008.

To assist in the discussions, a non-exhaustive list of suggested reading materials, as well as an introduction to the topic, have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum has been made available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

As a participant to the Open-ended Online Expert Forum on Risk Assessment and Risk Management, your contribution is of extreme importance in making this Forum an unprecedented medium of discussion which is a forerunner to the intergovernmental negotiations on the development of guidance material on specific aspects of risk assessment of LMOs.

The CBD Secretariat thanks you for your active participation. Happy discussions!

Best regards,

The Biosafety Division

RE: Welcome [#752] - posted on 2008-11-13 20:49 by Prof. Dr. Kazuo Watanabe

Dear all:

Finally, I could log in the thread.

My name is Kazuo Watanabe, working on LMO risk assessment, management and communication, at Gene Research Center, University of Tsukuba, Japan.

I am involved in RA on GM trees such as Eucalypts and poplar, and also have some informal consultation with tropical countries with their upcoming GM tree materials such as teak.

Both at CBD and Cartagena Protocol, forest biotechnology at large, become a subject for a discussion, but it shall be some preposition and common understanding background of what is forest biotech and how they could be used briefly before the RA on GM trees is discussed.

There are diverse opinions on GM trees in terms of association with biodiversity issues, but there shall be first of all, how the GM trees are intended to be used besides the elements and modality of measurements of risk assessments to be specifically discussed. Industry is considering the GM trees for commercial fields where usually are controlled for production such as plantation and this should not be mixed up by natural vegetation.

Prof. Dr. Kazuo Watanabe

B. Codifying common sense - again. Can we evaluate genetically modified trees? [#837] - posted on 2008-11-30 11:58 by Prof. Ron Sederoff

I am writing to address the conclusion raised by two contributors, who argued that due to the complexity of the nature of trees and their adaptation to the environment, it was not possible to make risk assessment of genetically modified trees, and therefore we should not try, or worse, yet, not be allowed to try. This issue was addressed nearly two decades ago, following discussions among government agencies, particularly, EPA, and USDA, on the prospects for regulating genetically modified organisms in agriculture and in the environment (see Bio/Technology 8, 1229 (1990) Codifying Common Sense, Douglas McCormick). In this article, several common sense principles were proposed for regulation. They still apply today to issues regarding genetically modified trees.

First, the article reiterated the argument, that the product, not the process should be regulated. This fundamental principle is still not widely accepted today, in spite of the strength of the science supporting it. Instead, the process is widely regulated, and justified by the invocation of the precautionary principle.

The article "Codifying Common Sense' sets out that regulation should begin with criteria based on what organisms and genetic modifications are considered safe now. We do not regulate traditional tree breeding, clonal forestry, tree hybridization, any cell and tissue culture procedures, trees derived by somaclonal variation, mutation breeding, or breeding or deployment of any exotic tree germplasm, once it passes quarantine and is in this country. Much is not known about the genetics of tree species and populations of forest trees, nonetheless, these introductions, selections and manipulations are unregulated.

Secondly, the nature of the modification should be considered. What is known about the mechanism of introduction, the genes themselves, the vector, the insertion site, and the expression of the construct. These issues are quite specific, and have in some cases, there is a high level of knowledge and confidence in what can be expected in a genetically modified plant. The risk can be evaluated in the context of the level of knowledge about natural mobile elements, producing insertions, transpositions, footprints, and altered gene regulation, widely throughout the organism. Plant genomes are dynamic and modification of sequence and position of genes and elements are natural forces for evolution and adaptation.

Third, what is the nature of the anticipated modification to the organism, and what would be the expected change to its growth, development, metabolism or adaptation. Such evaluations would vary in complexity, but some could be simply classified, as having an advantage under a particular condition, a disadvantage under such conditions, and in many cases, it could be argued that the change could be essentially neutral. Again, the baseline should be the relative effect compared to genes in natural populations, where many alleles are segregating, with advantageous, or deleterious effects, all subject to natural selection.

Finally, risk is to be balanced against the degree of containment. If containment can be applied, the risk that can be accepted should be higher than a case where, no containment is possible.

For forests, it must be remembered that many forests have dynamic histories. The lifetime of any population may have been short, and the history of human and natural intervention in forests has had dramatic consequences within relatively few tree generations. Particularly in North America, the temperate forests in the eastern USA have changed dramatically several times since the decline of the Wisconsin glaciation, due to competition, adaptation, the extent of fire, agriculture, pests and pathogens, and additional anthropogenic impacts on the land.

Yes, there is much we do not know about trees and forests. However, that does not preclude the application of common sense, when it comes to regulations that could apply to genetically modified trees.

Ron Sederoff
North Carolina State University (NCSU)
Ron_Sederoff@ncsu.edu

C. Transgenic trees - comments to the on-going discussion [#835] - posted on 2008-11-30 10:50 by Dr Marja Ruohonen-Lehto

My name is Marja Ruohonen-Lehto and I work as a Senior Adviser in the Finnish Environment Institute in Helsinki, Finland. I give expert advise to the competent authority and different ministries about biosafety and environmental risk assessment (ERA) of GMOs. I coordinate the small team at the institute that evaluates the ERA of national field releases and EU marketing applications. I have worked in this position since 1995.

Finland has had a few field releases on GM trees; two to be mentioned are the non-flowering modification in silver birch (*Betula pendula*) and the modification of carbon and nitrogen metabolism, also in silver birch. Both trials are small, strictly-confined trials (no flowering) that provide data on the growth behaviour, gene-expression, metabolic composition, herbivore behaviour and decomposition of detritus. In other words, data that can be used in risk assessment and is certainly very useful but must be considered in the context that it was derived from a confined, small-scale experiment.

68 % of Finland is covered by forest and 90 % of that is so-called production forest. The whole forest sector has a huge impact on Finland's economy but also biodiversity of our forests has gained a lot of attention during resent years. Several research programmes have been launched to investigate how to maintain biodiversity in our forests.

I have followed with great interest the discussions in this on-line forum. Many important issues have been brought up and I would like to add just a few comments.

1) We may already start to have plenty of experience with certain crop plants and certain inserted genes in them. But about the possible effects on biodiversity of modified trees (e.g. insect or fungal resistance or cold or draught tolerance), and especially if I may say so, modified forest trees is something we know very little about. Even if we can gain data on behaviour of certain genes in crop plants or even data on certain growth behaviour or metabolic changes in modified trees the estimation of possible long-term effects is hampered with considerable amount of uncertainty and lack of data. Basic research of forest ecology is still needed. Assessing long-living species like trees modelling is a tool that can be of great help and should be used. See e.g. work by Bjorn Tommeras and Jarle Tufto, Norway and Anna Kuparinen and co-workers, Finland.

2) ERA must be based on scientific knowledge. Identification of potential adverse effects is certainly value-laden to some extent (that can not be avoided) but even so the possible effects must be studied with sound scientific methods and well-designed experiments. Risk assessment is not a surrogate for basic research but must be based on basic research. How much uncertainty is acceptable is a political decision of each society and should not be mixed into the ERA. A scientist's or expert’s duty is to estimate the existing data, advice on how to gain more data if needed and try to evaluate the level of uncertainty that still exists.

A good example of how important it is to gather enough information was given in a talk by Professor Marvier at the last ISBGMO meeting in New Zealand about a week ago. She talked about meta-analysis of the effects of Bt crops on non-target organisms. She concluded that large open-access databases, that include data from all relevant RA studies is the future of risk assessment. I think this approach should be taken seriously into consideration.

D. Importance of a stepwise approach in the risk assessment of transgenic trees [#808] - posted on 2008-11-27 11:03 by Beatrix Tappeser

My name is Beatrix Tappeser. I am the head of division "GMO-regulation and Biosafety" at the Federal Agency for Nature Conservation, Germany

Forests are of great significance for humans from a socio-economic, an environmental and a cultural point of view. An important economic factor is the production and use of wood as an industrial and energy resource, while from an ecological perspective, the conservation of biological diversity and of ecological functions of forests are highlighted and connected with their sustainable use.

A number of ecological risks are being discussed concerning single traits of transgenic trees and their overall use. This discussion is based upon experience with genetically modified agricultural crops, which are commercially grown since the 1990s (e.g. herbicide tolerance and pest resistance), and ex-tended to include the special characteristics of trees and the complexity of forest ecosystems. With other traits, such as modified wood composition, however, no experience from other plants exists. Transgene escape through out-crossing and vegetative propagation is the most widely acknowledged risk connected with genetically modified trees (i.a. Williams & Davis 2005, DiFazio et al. 2004). Different approaches are being followed to prevent transgene escape by means of bio and gene technology (e.g. inhibition of pollen production, GURTs). Suppressing of pollen production, on the other hand, may have impact on pollinators and pollen feeders.

The identified risks of transgenic trees were compiled by several authors and are being discussed controversially, mostly since commercial use of transgenic trees has become possible and is being propagated for different reasons. However, studies addressing these identified and discussed risks of genetically modified trees by exemplified experiments under laboratory and greenhouse conditions are still widely missing. One the other hand, attempts are being made to prevent risks from the outset, including inhibition of the reproductive abilities of trees. Results of this research, however, show that stability of the transformed genotype is of special concern (i.a. Frankenhuysen & Beardmore 2004)

In general, there is still considerable uncertainty of potential impacts and risks of transgenic trees on biodiversity. Therefore, also considering the still deficient understanding of forest ecology and of the causes of plant invasions, frequently raised claims to approve the commercial use of transgenic trees must be considered premature. Also, existing regulations for genetically modified plants must be amended to include the special characteristics of trees. Application of the step-wise approach must be ensured also in the environmental risk assessment of transgenic trees, i.e. a decision on whether release experiments can be approved is only possible after appropriate assessments under laboratory and greenhouse conditions. Modelling approaches may be of special help (i.a. Farnum et al. 2007).

DiFazio SP, Slavov GT, Burczyk J, Leonardi S & Strauss SH (2004): Gene flow from tree plantations and impli-cations for transgenic risk assessment. Plantation Forest Biotechnology for the 21st Century.

Farnum P, Lucier A & Meilan R (2007) Ecological and population genetics research imperatives for transgenic trees. Tree Genetics & Genomes, 3, 119-133.

van Frankenhuyzen K & Beardmore T (2004): Current status and environmental impact of transgenic forest trees. Canadian Journal of Forest Research, 34, 1163-1180.

Williams CG & Davis BH (2005): Rate of transgene spread via long-distance seed dispersal in *Pinus taeda*. Forest Ecology and Management, 217, 95–102.

This is a reply to 808 RE: Importance of a stepwise approach in the risk assessment of transgenic trees [#829] - posted on 2008-11-28 17:16 by Dr Thomas Nickson

I am Tom Nickson, a scientist working in the area of environmental risk assessment for Monsanto Company for about 15 years. I would like to add to the idea of the "stepwise approach" used for environmental risk assessment.

Over the past 20 years, much has been learned about the process and conceptual basis that underpins environmental risk assessment. In my experience, one of the most significance challenges facing a risk assessor is discerning the amount of information needed for the risk assessment. Data requirements are dictated by the level of certainty required in the risk assessment, which is a matter of policy, not science. No matter what the object of the risk assessment is (trees, crops, fish, etc), overall guidance for the risk assessor is environmental protection goals set within policy, which determines what attributes of the environment are valuable, in need of protection and at what cost they will be protected. Typically, food and fibre production are an environmental attribute whose protection will be balanced against the desire for natural and urban areas.

As a developer of products improved through biotechnology, I have seen problems arising from not following a stepwise approach that begins with problem formulation (Raybould, 2006). However, I would also like to highlight another problem, which is the perception that science, particularly ecology, will define or describe "risk". Recently, Raybould (2007) has commented that risk assessment must have a structure grounded in policy. He described a commonly encountered problem as a conflict between an ecological versus and ecotoxicological approach. After reading many postings on these on-line forums, I feel it important to point out this distinction. Risk assessment should not be a surrogate for basic research. Public policy must guide the degree and even nature of data needed for decision-making, not a scientist or particular group versed in ecological theory. A risk assessment based in basic research does not serve the public since it creates excessive costs to the regulatory authority and developer, results in delays to introducing valuable products into the market and provides no great certainty in decision-making (Raybould, 2007).

Regardless of the LMO, I believe that environmental risk assessment should begin with proper problem formulation (Raybould, 2007). This critical first step enables risk assessors to use a guided process that is as efficient as possible, and ensures that sufficient data are collected for a decision based on reasonable certainty and guided by policy.

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

Raybould A (2007) Ecological versus ecotoxicological methods for assessing the environmental risks of transgenic crops. Plant Science: 173: 589-602

E. Experience with risk assessment of genetically modified (transgenic) trees [#764] - posted on 2008-11-17 06:34 by Hans Bergmans

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Risk Assessment of genetically modified (transgenic) trees, an example from the Netherlands

In the Netherlands we have up to this moment very limited experience with the environmental risk assessment of genetically modified trees. From this experience, however, we would like to present some thoughts that we hope are useful for the process of risk assessment for genetically modified trees.

It should be clear that our comments are presented as one would do this in an informal discussion between regulators and other interested parties, as points for discussion. They are not official standpoints of the Netherlands competent authority.

General considerations

As a point of departure we agree with the conclusion that was also drawn by the Canada-Norway Expert Workshop on Risk Assessment for Emerging Applications of Living Modified Organisms, that risk assessment of genetically modified trees can be done in a scientifically sound manner according to the methodology of Annex III of the Protocol (the report of the Canada-Norway workshop is included in the selected readings under the documents recommended by COP-MOP). The methodology of Annex III takes into account in the first step, inter alia, the specific characteristics of the receiving organism, the tree in this case. These characteristics are subsequently taken into account in the next steps.

The overall methodology of risk assessment of Annex III is a topic that will be discussed more extensively in the second session of this forum, when a further elaboration of the risk assessment process under Annex III of the protocol will be a topic for discussion.

Specific examples

At this moment there are two cases of deliberate release of transgenic trees in the Netherlands, one is an ongoing field trial (genetically modified apple trees expressing hordothionin), the other is an application for a field trial (genetically modified poplar trees with reduced lignin content)that is not yet permitted.

(1) Genetically modified apple trees expressing a hordothionin gene from barley (*Hordeum vulgare*).

Small scale confined field experiments with these trees have been permitted, under specific conditions (giberilin spraying to prevent flowering, and observation of effectiveness of this measure), to prevent outcrossing, so the potential effects of the field experiment will be restricted to the field plot where the apple trees have been planted.

Hordothionin expression is expected to lead to reduced sensitivity of the trees for fungal and bacterial infection. Hordothionin is known to have this function in barley, by reducing growth of fungi and bacteria. Thionins in general have this function in many plants.

From general experience with apple trees, it is not expected that reduced sensitivity to infectious disease will have a decisive impact on general fitness or invasiveness of apple, so no adverse effects on biodiversity are expected in this respect.

As another consideration, there may be effects on soil microflora, as those are the target organisms of hordothionin. The baseline experience is that no such effects have been observed for hordothionin in its natural environment, although we are familiar with barley in long term cultivation. It may be argued that in our agricultural practice barley will be cultivated in rotation with other crops, which may mask adverse effects to a certain extent. A typical effect of hordothionin expression in trees, e.g. in apples, would be that soil microflora would be exposed over longer continuous periods to hordothionin. In that respect, it might be interesting to see what effects are observed in no till cultivation of barley, as a baseline for a longer continuous period. Such data, if available, may be informative if at later stages of development of the transgenic apple trees larger areas will be planted in larger scale field experiments.

In the discussion on risk assessment, we focus on the potential adverse environmental effects, as they may arise from the deliberate release of the genetically modified trees into the environment. As we are dealing with a small scale field experiment in this case, we have not yet had extensive discussions on topics that may become important at later stages, such as changes in agronomic management, as these are not (yet) actual.

(2) A proposed field experiment with genetically modified poplar trees (*Populus* sp.), modified for reduced lignin content.

This is intended to be a small scale field experiment. The application is still under consideration.

In this case an OECD consensus document is available on the biology of poplar (http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/NT00002EC2/$FILE/JT00103743.PDF), which provides baseline information on the behaviour of poplar trees. A relevant important trait of poplar is that the trees are (normally) dioecious and obligatory outcrossing. Using female trees in a field experiment (as is done in this case) will reduce chances of outcrossing enormously, in the plants that are planted in the experiment.

What will be the most important area for discussion is the potential adverse effects that reduction of lignin content, the transgenic trait, may have on the interaction of the poplar trees with their environment: interactions with the (micro-) flora and fauna.

For this discussion we need to have knowledge of the baseline: an overview of the natural variation in lignin content within poplar species, and between species, and in general, between woody crops (and trees in general), and the typical environmental effects that various abundancy of lignin in crops will have, also compared to herbaceous crops; and on environmental effects that have been correlated with these variations.

The applicant of the field experiment has already provided information on these issues (e.g. the file attached to this contribution). At later stages it may be helpful if results of broader discussions on the trait of lignin content and its potential environmental effects would be available.

The so-called trait documents of OECD are a good source of this type of information, e.g. the document on safety information on transgenic plants expressing Bt toxins, for the Bt trait (http://www.olis.oecd.org/olis/2007doc.nsf/LinkTo/NT00002DF6/$FILE/JT03230592.PDF).

No OECD consensus document is available for lignin, however, and from experience we know that the drafting of such a document is not easy and takes a considerable time.

Still, it would be very useful to have documents available at an early stage of the risk assessment discussion, that provide scientifically sound overviews on the ecological impact of trees with reduced lignin content. Halpin et al. (Tree Genetics & Genomes (2007) 3:101–110) have recently published a paper on this subject, that may be a good start in this direction. This paper is added to this contribution.

halpin et al, ecological impacts of trees with modified lignin.pdf - 398 KB

This is a reply to 764 RE: Experience with risk assessment of genetically modified (transgenic) trees [#798] - posted on 2008-11-24 16:24 by Dr. Les Pearson

Resources available for risk assessments

My name is Les Pearson and I work for a small biotech company that does research on transgenic trees. I participated in the Norway/Canada workshop on risk assessment for emerging applications of LMOs, including trees. One of the conclusions of this meeting was that the general principles and methodologies of Annex III are appropriate for trees as for any other plant species.

With regard to conducting risk assessments for transgenic trees there are numerous resources available that provide background information as well as real-life examples of successfully competed risk assessments.

• Understanding the basic biology of the species is obviously a key starting point for any risk assessment. In his posting on this forum Hans Bergmans provided a link for the OECD Biology document for poplars. The following link provides a full listing of OECD Biology documents: http://www.oecd.org/document/51/0,3343,en_2649_34387_1889395_1_1_1_1,00.html, which cover a total of three genera plus seven additional individual species of trees. Those species being targeted for genetic modification are typically well studied and commonly used – even if no OECD document exists our experience has been that there is extensive scientific literature available to allow a good understanding of the basic biology of these species.

• The EU database of field trials/deliberate releases of GMOs (http://gmoinfo.jrc.ec.europa.eu/gmp_browse.aspx) typically includes a discussion of potential environmental impacts as well as any measures taken for the mitigation of risks. These provide insight and examples of the issues addressed during risk assessments for particular transgenic trees on a case-by-case basis. More than 50 trials have been approved representing a wide variety of tree species.

• In the US as of August 2008 over 700 field trials of woody species had been approved representing more than 40 species. While risks assessments were performed by USDA APHIS not all of these have been made publicly available. However, for field trials conducted under APHIS' Permit system there are a number of in-depth USDA APHIS environmental risk assessments available at http://www.isb.vt.edu/cfdocs/fieldtests1.cfm.

• USDA APHIS has also conducted a full environmental analysis for deregulation and commercial use of genetically modified plum and papaya (available at http://www.aphis.usda.gov/brs/not_reg.html). A recent draft analysis of a new papaya line has also been published (also available at the above site).

As with risk assessments for any plant species, this must be tailored to the characteristics of the tree species and the engineered trait. Across all of the above examples there is a good representation of different tree species and the key considerations that were addressed when performing risk assessments for a variety of transgenic trees.

This is a reply to 764 RE: Experience with risk assessment of genetically modified (transgenic) trees [#812] - posted on 2008-11-28 06:40 by Beatrix Tappeser

I would like to comment on a specific point of Hans Bergmans submission concerning the assessment of hordothionin-producing apple trees.

As we are doing comparative assessments defining a baseline (if possible) is a very important aspect. Hans Bergmans proposed to use the experience with no till barley as the parent organism as a starting point to assess possible impacts of hordothionin on soil microorganisms.

I think that would be not adequate given the huge differences between annual crop production and long living tree species. Especially the specific composition of mycorrhiza which is vital and important for different tree species cannot be compared to rhizosphere microbial composition of crop plants. Hordothionin is a compound naturally produced by barley. Risk assessment is meant to assess possible impacts in the new environment where a compound/plant is used. Taking the coevolved and adapted interaction would give a wrong picture.

F. Transgenic trees require a specific risk assessment procedure and considerations for relevance - comments on previous contributions [#799] - posted on 2008-11-24 17:05 by Prof Philippe Baret

Dear Sir/Madam,

As a member of the Belgian Biosafety Council, I was implied in the evaluation of poplar trees. I was also the supervisor of Gaetan Vanloqueren who achieved a thesis on "Innovation in the era of transgenic plants" (e.g. Vanloqueren and Baret, 2008).

I will comment on two aspects of the previous contribution of Hans Bergmans and Steve Strauss.

Concerning apple trees, I consider that

1. A risk assessment should be based on scientific data and not on « general experience ». Do we have clear data or model on the impact of transgenesis on general fitness and invasiveness? Both issues are rather complex and the level of uncertainties on long-term impact is high.

2. As we are dealing with a small scale field experiment in this case, we have not yet had extensive discussions on topics that may become important at later stages, such as changes in agronomic management, as these are not (yet) actual (quotation of Hans Bergmans). This situation is a very important issue. I don't understand why management and agronomic issues are not dealt with at early stages of the evaluation. Indeed, three reasons support an early assessment of these issues: 1) they require long term studies that should be started as early as possible, 2) they may help to design more precise risk assessment on specific aspects. It is difficult to assess risk for soils or ecosystems if the management and agronomical conditions are not determined, 3) agronomical considerations are important to define the relevance of the innovation.

3. In a specific study on apple trees (Vanloqueren, 2006), we showed that transgenic plants for disease resistance are not the only solution to this problem and that, in a problem-driven approach, more than twenty different strategies of innovations are possible. In a balanced cost-benefit approach, these different strategies should be compared.

Concerning poplar, I consider that :

4. My extensive field research with transgenic trees over the last 15 years :Dr. Strauss is a specialist of the production of transgenic plants and not a specialist of risk assessment. I really appreciate his contribution but there is some conflict of interest in this case, as Dr. Strauss produces transgenic poplars.

5. When considering specific novel modifications, it would be appropriate to consider the degree of novelty that is already practiced in breeding programs. The transgenic plant issue is not a question of novelty only. The public and political decision is to assess the transgenic plants. Our role, as experts, is not to discuss the opportunity of this evaluation. Our mission is to achieve this evaluation on a scientific basis.

6. Where a transgenic modification is clearly less novel than an accepted method of conventional breeding, it would be appropriate to exempt it from regulation entirely : I am very keen to know the definition of "less novel" (see also previous remark).

7. the possibility of evolutionary increase should not be assumed in risk assessment, given that most genetic manipulations are directed at highly managed environments such as plantations, not at success in the wild, and most genes for biotic stress resistance are unlikely to be sustainable given the rapid relative evolutionary rates of pest populations compared to that of wild or feral trees. : scientific references in support of these assertions will be very welcome. If the affirmation on evolutionary rates is true, I don't see the interest of producing transgenic trees.

8. Finally, with respect to small and short term field trials (e.g., below 10 to 100 hectares, below 10 years), the scale of possible release if often so small that the likelihood of adverse impact is extremely low and remote, even if there is a small release of seeds or pollen. However, where provisions for harvest prior to flowering occur, or harvest of trees in the vicinity of the trial occurs (and thus most matings and regeneration), the release is almost nil compared to conventional breeding. Strict regulations of field trials are therefore inappropriate, especially given their critical importance for risk assessment research, as discussed below. Unfortunately, in an ecosystem, there is no strict relationship between the scale and the effect. In invasiveness for example, there is many example of large-scale ecological damages due to a minuscule initial event.

9. Models are essential for risk assessment - The combination of field data to calibrate models, and models that take into account realistic details of the environment, genes, traits, fitness, demography, etc can provide very useful estimates of the range of risk possible over decades to centuries. Sensitivity analysis allows the reliability of the model to be directly assessed. See the work by DiFazio cited below for one example. This allows investigations of risk scenarios that extend far beyond experimental time frames for trees. I fully agree but the models do not require data from trials with transgenic plants. A calibration is possible with normal plants or data from confined trials (in greenhouses for example). As transgenic related risk is in many respect irreversible and considering the specific characteristics of trees (long term production of pollen, large scale plantations, monitoring on very long periods), model-based risk assessment have to be an absolute prerequisite before any kind of trial (small or large scale).

Trees have specific plant species: their lifespan may exceed the lifespan of human experimenters, they are planted in large area, they are impossible to isolate from the wild ecosystems, they have a major impact on biodiversity. Considering these specificities, they require the development of specific procedure including the use of models prior to any outdoor dissemination and an early assessment of the relevance of the proposed modification.

These remarks reflect my personal views and are not made on behalf of the Belgian Biosafety Council.

As I am not associated with industries producing transgenic plants and I am not contributing to the molecular or biotechnological aspects of transgenic plants, I declare that I have no conflict of interest considering the risk assessment of transgenic plants.

Philippe Baret, Professor at the Universite de Louvain (Louvain-la-Neuve, Belgium)

Vanloqueren G., Baret P.V. (2008)

Why are ecological, low-input, multi-resistant wheat cultivars slow to develop commercially? A Belgian agricultural ‘lock-in’ case study.

Ecological Economics 66:436-446

Vanloqueren, G., Baret, P.V. 2004

Les pommiers transgéniques résistants à la tavelure - Analyse systémique d'une plante transgénique de "seconde génération".

Le Courrier de l’Environnement de l’INRA (52):, Septembre 2004.

This is a reply to 799 RE: Transgenic trees require a specific risk assessment procedure and considerations for relevance - comments on previous contributions [#801] - posted on 2008-11-25 05:09 by Hans Bergmans

I would like to submit some comments regarding the contribution of Prof. Baret:

By and large I agree with his comments, the main question is how to do risk assessment of field experiments at early stages, and how to initiate the risk assessment research the results of which will be needed later on.

Indeed, in the example that I gave, quoted in paragraph 2 of Prof. Baret, we are dealing with a small scale field experiment, and according to our regulations we do a risk assessment of the field experiment as such. I have indicated that a number of discussions will become actual at later stages, and we will take them into account when risk assessment of larger scale longer term field trials become actual.

That does not preclude that we can, and probably should, have these discussions now already, it just means that these discussions at this stage do not influence the risk assessment of the small scale short term field trial. This should be assessed on its own merits.

I fully agree that it will probably only be possible to perform a risk assessment of larger studies that last for a longer period, if relevant empirical data are available. Necessary studies may take a long time, and applicants that want to perform larger and longer studies should take that into account. Governments may start the discussion on risk assessment of these cases early, and may consider if they want to fund risk assessment research for certain topics that they think are important (as we did for instance in our ERGO <http://www.nwo.nl/nwohome.nsf/pages/NWOA_6JNP94_Eng> project).

But all this does not directly influence the risk assessment of a specific small scale field experiment, even if we agree with the comments in paragraph 8, that small scale field experiments are not always as useful for collecting empirical data on the ecological behaviour of the transgenic trees. The impact of the experiment will be negligible anyhow. It is up to the applicant however to decide if he wants to perform a small scale field experiments to evaluate characteristics of the GMO under field conditions. This is also an appropriate way forward in traditional breeding.

Whether strict regulations are appropriate or not is dependent on the outcome of the discussion how the conclusions of the discussion of precautionary approach for this case. Different competent authorities may reach different conclusions here.

But it is obvious that risk assessment research studies should be done under circumstances that meaningful answers for risk assessment can be generated. And indeed, as Prof. Baret mentions in paragraph 9, many very relevant studies can be done with non-GMO trees, which would evade problems of permitting large scale GMO field experiments.

This is a reply to 801 RE: Transgenic trees require a specific risk assessment procedure and considerations for relevance - comments on previous contributions [#806] - posted on 2008-11-26 15:38 by Dr. Les Pearson

I just wanted to add a point of clarification to this discussion. In a few places the phrase ‘risk assessment research’ has been used. Research is – or should be – aimed at testing a specific hypothesis. On the other hand, risk assessment is a process or procedure. The procedure itself may not change under different circumstances, but the specific factors addressed and relevant information would differ on a case-by-case basis. Research can provide data or information on specific aspects of trees that could be useful in a risk assessment, and presumably this is the kind of research to which this phrase is referring. However, we should be careful that this phrase is not confused with a concept of doing research to test the hypothesis that there is or is not a risk. Nothing is without risk, yet most people (perhaps thankfully) are unaware of

the risks that they take routinely every day. Risk assessments use the available data to gain an understanding of possible outcomes, and estimates of whether these are likely or unlikely. The reality is that for any situation there can never be complete or perfect information. Based on the risk assessment, decisions can then be made on a particular course of action (risk management) – in this case perhaps, to allow a field trial to proceed or not.

G. Comments on risk assessment and field trials from Professor S. Strauss, USA [#772] - posted on 2008-11-18 19:35 by Steven Strauss

My comments are inserted and also attached as a pdf

Comments on risk assessment of transgenic trees

Steven H. Strauss, Distinguished Professor

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Steve.Strauss@OregonState.Edu

Dear Sir/Madam

I wish to offer the following comments and observations as you seek information on risk assessment of transgenic trees. I have studied risk assessment of transgenic trees for approximately 20 years, and two of the background papers for this discussion were in fact produced by my laboratory (DiFazio et al, James et al). You can see my full qualifications here: http://www.cof.orst.edu/coops/tbgrc/Staff/strauss/index.htm

My extensive field research with transgenic trees over the last 15 years, which has included well above 100 USDA APHIS authorized field trials and two permits in the USA, has shown me how costly and onerous the current regulations are for scientific research, even in the USA. Although I support careful, science based risk and benefit assessments of transgenic trees, because I believe that additional stringent requirements for risk assessment are very likely to foreclose most additional field research (and FIELD research is essential for most kinds of reliable risk assessment data), I emphasize the relaxation of regulations and requirements for detailed risk assessment studies in cases where the level of genetic novelty is low.

Because much of the discussion seeks to clarify the specific intents of Annex III, I start by commenting on several of its principles. My comments follow each quoted principle/provision.

1) "General principles /. 5. Risks associated with living modified organisms or products thereof…should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment."

I believe that "context" is the key consideration in risk assessment. Every genotype in a breeding program has some risk of an adverse outcome for biodiversity depending on point of view and to what it is compared. To do a risk assessment without a specific frame for comparison makes no scientific sense. I believe that the CBD should require that all risk assessments be conducted with explicit comparisons to conventional breeding programs and methods, both in general and specific to the tree taxon and environment in question. If a general method is viewed as safe for many crops, such as is chemical mutagenesis, then there is little reason to expect this consequence of the genetic engineering process to be unsafe for transgenic trees. When considering specific novel modifications, it would be appropriate to consider the degree of novelty that is already practiced in breeding programs. For example, a program that makes extensive and legal use of exotic species and inter-species hybrids would have a much higher

threshold for novelty than would a program that only uses local, natural genetic variation. It would not be difficult, for example, to conduct simple chemical or biological assays to determine relative novelty (e.g., by testing a range of genotype from conventional breeding against a panel of herbivores/microbes, and compare it to the effect of a transgenic type).

Where a transgenic modification is clearly less novel than an accepted method of conventional breeding, it would be appropriate to exempt it from regulation entirely. This concept fits with the methodology provision "7. The process of risk assessment may on the one hand give rise to a need for further information about specific subjects, which may be identified and requested during the assessment process, while on the other hand information on other subjects may not be relevant in some instances." Where a modification is modest or similar in comparison to conventional breeding effects, there would be no need to require additional information on its specific effects.

Likewise, for transgenic trees that have modified natural traits based on native or functionally homologous genes (e.g. those for plant metabolic pathways and hormones), a toxicology approach to risk assessment does not make sense, as there is no novel toxin to test. These plants do not have novel toxic properties, just modifications to native plant processes that make them more useful or productive in plantations, similar to the effects of conventional breeding—which have effects on general plant chemistry, but do not introduce major new toxicological novelties.

Under context, it is also important to consider the larger picture, not just specific ecological effects, in risk assessment. For example, if a transgenic tree is more productive and can thus lead to plantings that produce more wood on a smaller area, this can have a large indirect benefit for biodiversity—as has been seen in many countries already. The well known paper by Sedjo and Botkin (1997, "Using forest plantations to spare natural forests," Environ. Health Perspect. 39:15-20), made this point powerfully. Clearly, the indirect risks of not using gene technology for its beneficial effects on biodiversity may greatly outweigh most of the direct risks from specific genes and genotypes. I believe that such "opportunity cost" types of risks to biodiversity (e.g., where risk assessment data requirements are so great as to result in loss of technology development) should be explicitly considered in risk assessment protocols adopted by the CBD. This is a serious concern for transgenic trees as many years of field trials, in many places, are often required to generate data, yet field trials are extremely costly and often restricted or impossible due to national regulations. The stringency of regulation for transgenic trees makes this a real programmatic-level environmental risk that should be explicitly considered.

2) "General principles / 6. Risk assessment should be carried out on a case-by-case basis. The required information may vary in nature and level of detail from case to case, depending on the living modified organism concerned, its intended use and the likely potential receiving environment."

The need to tailor data requirements, and regulations for field research, to the specific modifications made is critical. As genomic knowledge of trees progresses, more and more transgenic tree products under development will not contain novel genes or proteins as their "active ingredients," but only native or highly homologous forms whose regulation has been modified. Of course, such genetic variation in regulation of native genes is also extensive in nature. Thus, such modified forms clearly do not require the same scrutiny as, for example, forms with a novel ecotoxic gene from a different kingdom. In fact, many such forms might be exempted from regulation as they are generally BETTER known than the products of many types of conventional breeding, whose gene-level causes of modified properties are unknown or very poorly known. And the variation in the target traits, such as rate of growth or tissue quality, is also extensive in wild samples, which as discussed above should be explicitly considered as context.

This concept fits well with the provision under methodology "8. (a) An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity…" This implies that modifications that are not biologically novel, would require much less scrutiny, or be exempt from regulation. Cis-genic (same species), intra-genic

(same genus), and homo-genic (same biological function) types of modifications are examples of classes that might be exempt or in a much reduced scrutiny category.

Note that this suggested fine tuning of risk assessment requirements to the biological risks of different types of cases is a form of case-by-case assessment, however, it also benefits from the recognition of distinct biological categories of novelty and genetic familiarity.

A similar provision would be to exempt, or put in low risk categories, those genes that are foreign to trees but are already in wide use in the environment, and have undergone extensive risk assessment in other plant species. This includes some of the selectable marker and reporter genes, and some promoter and other regulatory elements, already in extensive use in transgenic crops. This point was argued in detail by Bradford et al, (2005, "Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology, and genomics," Nature Biotechnology 23:439-444). They also discussed how very small releases, and genes with expected domestication effects (neutral or deleterious to fitness in the wild), should be put in low risk or exempt categories, which I also strongly support. Examples are reduced fitness trees as a result of reduced or modified lignin, reduced reproductive fertility, increased reliance on intensive management (fertilization, water) for growth improvement, and reduced height relative to diameter growth.

3) "Methodology 8. (b) An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism; (c) An evaluation of the consequences should these adverse effects be realized; (d) An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized;"

These provisions emphasize that is the adverse ecological effects, not the simple movement and presence of a transgene, that should be the only focus of risk assessment. Large scale movements of pollen, seed, or vegetative propagules—but that give rise to extremely low frequencies of presence, or have very small ecological impacts compared to conventional breeding and silviculture (with its many genotypes, species, and management/harvest effects)—should explicitly NOT be considered an adverse effect in risk assessments under the CBD, no more than such movement is considered a harm in conventional breeding. Likewise, the possibility of evolutionary increase should not be assumed in risk assessment, given that most genetic manipulations are directed at highly managed environments such as plantations, not at success in the wild, and most genes for biotic stress resistance are unlikely to be sustainable given the rapid relative evolutionary rates of pest populations compared to that of wild or feral trees. In other words, fitness benefits are very likely to be much reduced over a small number of generations for trees, greatly restraining the speed and extent of increase in transgene frequency that might occur in wild or feral trees.

Finally, with respect to small and short term field trials (e.g., below 10 to 100 hectares, below 10 years), the scale of possible release if often so small that the likelihood of adverse impact is extremely low and remote, even if there is a small release of seeds or pollen. However, where provisions for harvest prior to flowering occur, or harvest of trees in the vicinity of the trial occurs (and thus most matings and regeneration), the release is almost nil compared to conventional breeding. Strict regulations of field trials are therefore inappropriate, especially given their critical importance for risk assessment research, as discussed below.

Finally, I wish to stress two points:

Field trials are essential for risk assessment

As alluded to above, Field trials must be enabled, not restricted—because it is only in the field that risks can be evaluated, and the degree of ecological novelty due to a transgene estimated in comparison to conventional causes of ecological variation (selected varieties, silvicultural and harvest practices, etc).

The reason field studies are needed is that tree ecophysiology and chemistry is very different in the field compared to the lab or greenhouse. Thus, risk assessments depend on a reasonable, affordable, efficient regulatory framework that permits a great deal of field research. The CBD therefore has a direct interest in seeing that its negotiations do not give rise to regulations that further restrict the ability of participating countries to do large numbers of field trials.

Models are essential for risk assessment.

The combination of field data to calibrate models, and models that take into account realistic details of the environment, genes, traits, fitness, demography, etc can provide very useful estimates of the range of risk possible over decades to centuries. Sensitivity analysis allows the reliability of the model to be directly assessed. See the work by DiFazio cited below for one example. This allows investigations of risk scenarios that extend far beyond experimental time frames for trees.

OUR PUBLISHED WORK SUPPORTS THESE GENERAL RISK ASSESSMENT PRINCIPLES. ALL PAPERS CAN BE DOWNLOADED HERE: http://www.cof.orst.edu/coops/tbgrc/Staff/strauss/publications.htm

TRANSGENIC TRAITS ARE HIGHLY STABLE IN TREES

Li, J., A.M. Brunner, R. Meilan, and S.H. Strauss. (2008) Matrix attachment region elements have small and variable effects on transgene expression and stability in field-grown Populus. Plant Biotechnology Journal 6: 887-896

Li, J., A.M. Brunner, O. Shevchenko, R. Meilan, C. Ma, J.S. Skinner, and S.H. Strauss. (2008) Efficient and stable transgene suppression via RNAi in field-grown poplars. Transgenic Res.17: 679-694. DOI 10.1007/s11248-007-9148-1

Li, J., R. Meilan, C. Ma, M. Barish, and S.H. Strauss. (2008) Stability of herbicide resistance over 8 years of coppice in field-grown, genetically engineered poplars West. J. Appl. For. 23(2): 89-93

Li, Jingyi (2006) Jingyi Li for the degree of Doctor of Philosophy in Forest Science presented on September 20, 2006. Title: Stability of Reporter Gene Expression and RNAi in Transgenic Poplars over Multiple Years in the Field under Vegetative Propagation.

Strauss, S.H., Brunner, A.M., Busov, V.B., Ma, C., and Meilan, R. (2004) Ten lessons from 15 years of transgenic Populus research. Forestry, 77(5) 455-465

Meilan, R., Auerbach, D.J., Ma, C., DiFazio, S.P., and Strauss, S.H. (2002) Stability of herbicide resistance and GUS expression in transgenic hybrid poplars (Populus sp.) during several years of field trials and vegetative propagation. HortScience,37(2) 277-280

MODELS ARE VALUABLE AND USEFUL FOR RISK ASSESSMENT

Brunner, A., J. Li, S. DiFazio, O. Shevchenko, R. Mohamed, B. Montgomery, A. Elias, K. Van Wormer, S.P. DiFazio, & S.H. Strauss. (2007) Genetic containment of forest plantations. Tree Genetics & Genomes, 3:75-100 DOI 10.1007/s11295-006-0067-8 (Strauss is co-senior author)

DiFazio, S.P., Slavov, G.T., Burczyk, J., Leonardi, S., and Strauss, S.H. (2004) Gene flow from tree plantations and implications for transgenic risk assessment. In C. Walter and M. Carson (eds.) Plantation Forest Biotechnology for the 21st Century. Research Signpost, Kerala, India. 405-422

Slavov, G.T., DiFazio, S.P. and Strauss, S.H. (2004) Gene flow in forest trees: gene migration patterns and landscape modelling of transgene dispersal in hybrid poplar.. In H.C.M. den Nijs, D. Bartsch, and J.

Sweet (Eds.), Introgression from genetically modified plants into wild relatives, , Pp 89-106. CABI Publishing, Cambridge, MA, USA.

DiFazio, S.P. (2002) Stephen P. DiFazio for the degree of Doctor of Philosophy in Forest Science presented on January 7, 2002. Title: Measuring and modeling gene flow from hybrid poplar plantations: Implications for transgenic risk assessment.

MUTAGENESIS, FAMILIAR TRAITS, DOMESTICATION TRAITS, AND MODIFICATIONS TO NATIVE GENES MERIT EXEMPTION OR MUCH LOWER SCRUTINY COMPARED TO GENES THAT IMPART NOVEL ECOTOXIC PROPERTIES

Bradford, K.J., Van Deynze, A., Gutterson, N., Parrot, W., and Strauss, S.H. (2005) Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology, and genomics. Nature Biotechnology, 23 (4) 439-444

Strauss, S.H. (2003) Genomics, genetic engineering, and domestication of crops. Science, 300 61-62

VERY HIGH LEVELS OF CONTAINMENT ARE FEASIBLE WITH SUFFICIENT FIELD RESEARCH TO DEVELOP AND TEST CONTAINMENT GENES

Brunner, A., J. Li, S. DiFazio, O. Shevchenko, R. Mohamed, B. Montgomery, A. Elias, K. Van Wormer, S.P. DiFazio, & S.H. Strauss. (2007) Genetic containment of forest plantations. Tree Genetics & Genomes, 3:75-100 DOI 10.1007/s11295-006-0067-8 (Strauss is co-senior author)

Skinner, J.S., Meilan, R., Ma, C., and Strauss, S.H. (2003) The Populus PTD promoter imparts floral-predominant expression and enables high levels of organ ablation in Populus, Nicotiana and Arabidopsis. Mol. Breed., 12 119-132

Meilan, R., Brunner, A.M., Skinner, J.S., and Strauss, S.H. (2001) Modification of flowering in transgenic trees. In N. Morohoshi and A. Komamine (Eds.), Molecular Breeding of Woody Plants, , Pp 247-256. Elsevier Science B.V.

EXTENSIVE FIELD TRIALS ARE NEEDED FOR RISK ASSESSMENT STUDIES

Valenzuela, S., and Strauss, S.H. (2005) Lost in the woods. Nature Biotechnology, 23 532-533

Brunner, A.M., Busov, V.B., and Strauss, S.H. (2004) Poplar genome sequence: functional genomics in an ecologically dominant plant species. Trends in Plant Sci, 9:49-56

Strauss, S.H., and Brunner, A.M. (2004) Tree biotechnology in the 21st century: Transforming trees in the light of comparative genomics. In S.H. Strauss and H.D. Bradshaw (Eds.), The BioEngineered Forest: Challenges to Science and Society, , Pp 76-97. Resources for the Future, Washington, D.C., USA.

Campbell, M.M., Brunner, A.M., Jones, H.M., and Strauss, S.H. (2003) Forestry's Fertile Crescent: The application of biotechnology to forest trees. Plant Biotech. J., 1 141-154.

Strauss, S.H., DiFazio, S.P., and Meilan, R. (2001) Genetically modified poplars in context. For. Chron., 77(2) 271-279.

H. Guidance on risk assessment for Genetically modified trees [#762] - posted on 2008-11-16 11:31 by Dr Ossama Abdel-kawy

According to the FAO (2004), "A regulatory framework to govern research and application of genetically modified forest trees on a case-by-case basis is essential. The issue goes beyond the country level, since

pollen flow and seed dispersal do not take account of national boundaries, and since wood is a global commodity." Thus an international framework to assess the safety of GM trees before their environmental release is necessary. The FAO adds, "… it is very important that environmental risk assessment studies are conducted with protocols and methodologies agreed upon at national and international levels. It is also important that the results of such research are made widely available."

The available literature on risk assessment of GM trees is quite limited. Much of the published work is focused on the research and development and trait improvement aspects rather than risk assessment. Some selected literature related to risk assessment is highlighted here (obtained from the International Centre for Genetic Engineering and Biotechnology (ICGEB) 'Biosafety Database') (http://www.icgeb.org/~bsafesrv/db/biosafety.html). A few field studies on the effects of transgenic poplar to non-target organisms and gene flow were carried out in China.

1.Mullin, T.J. and Bertrand, S. 1998. Environmental release of transgenic trees in Canada - potential benefits and assessment of biosafety. Forestry Chronicle vol. 74 (2): p.203-219.

2.Lu Meng Zhu, Han Yi Fan and Du Sheng Ming. 1999. Risk assessment and safety management of genetic engineered trees. Forest Research vol. 12 (3): p.325-331.

3.Sampson, V. and Lohmann, L. 2000. Can't see the trees for the wood. Seedling vol. 17 (3) p.2-13.

4.Yanchuk, A. 2002. The role and implications of biotechnology in forestry. Forest Genetic Resources (No.30) p.18-22. ftp://ftp.fao.org/docrep/fao/005/y4341e/y4341e00.pdf

5.Van Frankenhuyzen, K..2004. Current status and environmental impact of transgenic forest trees. Canadian Journal of Forest Research vol. 34 (6) p.1163-1180. http://dx.doi.org/10.1139/x04-024

Strauss, S. H. and Bradshaw, H. D. (eds) 2004. The bioengineered forest: challenges for science and society. Resources for the Future, Washington, USA

Hancock, J. F. and Hokanson, K. 2004. Invasiveness of transgenic versus exotic plant species: how useful is the analogy? In Strauss and Bradshaw (eds). The bioengineered forest: challenges for science and society p.181-189. Resources for the Future, Washington, USA.

Johnson, B. and Kirby, K. 2004. Potential impacts of genetically modified trees on biodiversity of forestry plantations: a global perspective. In Strauss and Bradshaw (eds). The bioengineered forest: challenges for science and society p.190-207. Resources for the Future, Washington, USA.

Raffa, K. F. 2004. Transgenic resistance in short-rotation plantation trees: benefits, risks, integration with multiple tactics, and the need to balance the scales. In Strauss and Bradshaw (eds). The bioengineered forest: challenges for science and society p.208-227. Resources for the Future, Washington, USA.

Burdon, R. D. and Walter, C. 2004. Exotic pines and eucalypts: perspectives on risks of transgenic plantations. In Strauss and Bradshaw (eds). The bioengineered forest: challenges for science and society p.52-57. Resources for the Future, Washington, USA.

Hoenicka, H. and Fladung, M. 2006.Biosafety in Populus spp. and other forest trees: from non-native species to taxa derived from traditional breeding and genetic engineering. Trees: Structure and Function vol. 20 (2) p.131-144. http://dx.doi.org/10.1007/s00468-005-0023-5

Valenzuela, S., Balocchi, C. and Rodríguez, J. 2006. Transgenic trees and forestry biosafety. Electronic Journal of Biotechnology vol. 9 (3) p.335-339. http://dx.doi.org/10.2225/vol9-issue3-fulltext-22

Wang JH, Zhang JG, Hu JJ, Zhang Z, Zhang SG (2004) Studies on safety assessment of transgenic Bt poplar. China Biotechnol 24:49-52

Hu JJ, Zhang YZ, Lu MZ, Zhang, JG, Zhang SG (2004) Transgene stability of transgenic Populus nigra and its effects on soil microorganism. Scientia Silvae Genetica 40:105-109

Zhang Z, Wang JH, Zhang JG, Zhang SG (2004) Effects of transgenic poplars to the structures of insect community. Scientia Silvae Sinicae 40:84-89

Yang MS, Lang HY, Gao BJ, Wang JM, Zheng JB (2003) Insecticidal activity and transgene expression stability of transgenic hybrid poplar clone 741 carrying two insect-resistant genes. Silvae Genetica 52:197-201

Gao BJ, Zhang F, Hou DY, Wu BJ, Zhang SP, Zhao XL (2003) Structure of arthropod community in stands of transgenic hybrid poplar 741. J Beijing Forest University 25:62-64

Lu M. Z., X. L. Chen J. J. Hu. Empirical assessment of gene flow from transgenic poplar plantation. In Proceedings of 9th International Symposium on the Biosafety of Genetically Modified Organisms[R], Jeju Island, Korea. 2006.

TOPIC 3 - RISK ASSESSMENT AND RISK MANAGEMENT OF TRANSGENIC MICROORGANISMS AND VIRUSES.

Introduction to the topic

by Kaare Magne Nielsen, Department of Pharmacy, University of Tromsø, Tromsø, Norway. E-mail: knielsen@farmasi.uit.no

The basis for risk assessments (RA) is the knowledge available and its quality denominators, the use of inferences where necessary, and a transparent treatment of the identified uncertainties and knowledge gaps. A key challenge is to communicate how these conditions define the strength of the risk conclusions drawn; as conclusions cannot be stronger than the evidence behind. Often, uncertainties are of a qualitative nature and it is scientifically flawed to present risk conclusions on a quantitative scale when the underlying biological processes and uncertainties are not understood numerically. The influence of assumptions and inferences in RA outcomes needs to be more transparently communicated.

Scientific knowledge production and, hence, RA may be value influenced (e.g. subjective bias in risk hypothesis formulation, question framing and data interpretation). Stringent measures need to be developed to effectively identify values inherent in RA. A recent editorial in Nature Biotechnology (2008, p. 1051) points to that researcher biases/motivations influence study outcomes and, hence, the unmet need for independent research and information sources. RA procedures lack efficient tools to adequately deal with study biases. The question is not how to discard values from the process, but how to appropriately recognize them in a transparent manner so that the globally diverse approaches to GMMV can be most effectively understood, harmonized and made operational.

The initial risk characterization process consists of the following steps:

a. hazard identification,
b. hazard characterization, and
c. Exposure assessment.

In the on-line discussions, it is necessary to explicitly communicate the step and process that is discussed. It will also be useful to distinguish between the RA components of intended versus unintended effects, and considerations of sources of uncertainty, indeterminacy and ignorance.

Categorically, the GMMV products can be divided into:

i) purified products derived thereof,
ii) inactivated products that have no replication or DNA transfer potential, and
iii) Products with replication potential.

These categories of products generate different biosafety questions that can initially be structured using the concepts of familiarity and substantially equivalence. The comparative approach requires that suitable comparators can be found. Identifying a relevant comparator may, however, be challenging or impossible. This on-line discussion offers an opportunity for the identification and development of alternatives to the concepts of familiarity and substantial equivalence.

Some key biosafety considerations of live GMMVs are the likelihood of:

i) Undesired ecosystem interactions/impacts due to unintended survival, spread and persistence of GMMV,
ii) Undesired heritable biological system impacts caused by horizontal gene transfer (HGT) of the novel genetic modification to new recipients, or caused by HGT/recombination of the GMMV with wildtype genomes leading to e.g. altered host range and dispersal dynamics of the GMMV itself.

A crucial point is potential irreversibility. The limited understanding of key environmental processes presents a challenge to RA of GMMV. For instance, to fully understand the genetic impact of novel GM traits in live MVs, questions such as those listed below must be answered: What are the drivers of natural MV diversity, dynamics, and evolution? Do we know how the various drivers interact to shape genetic diversity in a given environment? Which existing genes in the current gene pool will survive or are on the way to extinction? How will these processes affect future community structure and composition? These questions can perhaps be addressed for most GM-plants but not for GMMVs. A mechanistic knowledge of the cell cytoplasm can be constructed today by using “omics” technologies but the ecosystem roles and interactions of live GMMV remain fragmented, descriptive and with little functional contextualization.

The overall key determining potential unintended impacts of live GMMV is selection; the ultimate determinant of long-term survival of GMMV or disseminated GM DNA. Relative and absolute fitness considerations are therefore required in RAs along with relevant tempo-spatial population dynamic considerations.

The knowledge gaps introduced above call for the use of minimal sized GM inserts, broader knowledge of selection, and understanding of the fitness changes caused by the GM trait when present in the intended recipient or in new recipients after HGT. Depending on the category and products of the GMMV assessed, careful considerations of relevant biological, ecological and evolutionary scales are needed. By doing so, questions will arise as to if quantitative descriptors can be found and to what extent researcher motivation and biases influence data quality through study design, outcome interpretation and reporting.

Suggested points for discussion

- How to apply Annex III when assessing the risks of transgenic microorganisms and viruses;
- Experience in conducting risk assessment of transgenic microorganisms, including but not limited to those for bioremediation, industrial applications, food and feed production, biocontrol, diagnostic kits and veterinary pharmaceuticals;
- Difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc.;

- Elements necessary to conduct risk assessments of transgenic microorganisms;
- Issues that are unique to this topic;
- Recommendations for preparing risk assessment reports.

List of threads and number of replies

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B. Risk assessment of microorganisms and viruses released into the environment	0
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D. How to apply Annex III when assessing the risks of transgenic microorganisms and viruses	0
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Interventions

A. Welcome [#742] - posted on 2008-11-09 22:04 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Risk assessment and risk management of transgenic microorganisms and viruses".

The discussions within this group will take place during 10-23 November 2008.

To assist in the discussions, a non-exhaustive list of suggested reading materials, as well as an introduction to the topic, have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum has been made available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

As a participant to the Open-ended Online Expert Forum on Risk Assessment and Risk Management, your contribution is of extreme importance in making this Forum an unprecedented medium of discussion which is a forerunner to the intergovernmental negotiations on the development of guidance material on specific aspects of risk assessment of LMOs.

The CBD Secretariat thanks you for your active participation. Happy discussions!

Best regards,

The Biosafety Division

This is a reply to #742 RE: Welcome [#745] - posted on 2008-11-11 08:14 by 魏伟

It is fine to sign in and to be able to post reply here. I noticed that the main topic here is related to biosafety of transgenic fish. Is there any experts working on fish? I work with plant only and focus on the geneflow from transgenic crops to the wild relatives and the following ecological consequence.

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B. Risk assessment of microorganisms and viruses released into the environment [#841] - posted on 2008-11-30 17:34 by Dr Esmeralda Prat

My name is Esmeralda Prat, I work for a biotechnology developer as biosafety manager and I am active in the European Biosafety Association.

My understanding is that this section treats mainly the risk assessment of living microorganisms and viruses released into the environment. These may be used in live animal vaccines, environmental remediation, etc.

Kaare Magne Nielsen talked about purified products derived of microorganisms or viruses and inactivated products that have no replication or DNA transfer potential. My understanding is that those two cases are outside the scope of the protocol that addresses Living Modified Organisms.

Annex III of the Protocol is a good starting point to evaluate and then manage the risk of release of live microorganisms and viruses on a case by case basis as well as to take into consideration the public health and environmental benefits that some of these applications may bring.

C. Release of the transgenic microorganisms and viruses [#775] - posted on 2008-11-20 06:43 by Shigeki Inumaru

It is almost impossible to get a clear grasp of the distribution of microorganisms and viruses, once they are released into the field. Therefore it should be restricted to only the transgenic microorganisms and viruses which are neither infect nor proliferate in the natural environment. (It is all right that an inoculated transgenic microorganism or virus is proliferates only in the individual organism.) Otherwise we cannot manage the risks of the transgenic microorganisms and viruses.

My comment may not be appropriate, since it is uncertain for me what should be discussed in this forum. Forgive me, if so.

Shigeki Inumaru
National Agriculture and Food Research Organization
National Institute of Animal Health

This is a reply to 775 RE: Release of the transgenic microorganisms and viruses [#833] posted on 2008-11-29 18:28 by Jack Heinemann

I would add to Dr. Inumaru's comment that in addition to the great gap of knowledge we have about the diversity of microorganisms (including viruses) is the great gap of knowledge we have about their

biology. As a microbiologist, I would be very hesitant to argue that I could guarantee that any virus would only transfer to recipients of a particular defined species range. While we may be pretty sure that some virus types presently include no individuals that cause disease outside of a defined species range, transfer is a very different, and much more difficult, standard to prove. Some hazards arise simply from transfer, not from the completion of a particular disease-associated lifecycle.

I would also be hesitant to conclude that viruses projected to be unable to propagate outside of the laboratory will always be unable to do so, particularly when they may come within recombination-distance of the very many unknown, non-disease causing viruses transferring through the same host.

D. How to apply Annex III when assessing the risks of transgenic microorganisms and viruses [#758] - posted on 2008-11-14 15:36 by Leticia Pastor Chirino

My name is Leticia Pastor Chirino, I am the Head of the Authorization Department of the National Centre for Biological Safety in Cuba. In the case of Cuba the risk assessment process is undertaken according to the Resolution 180/2007 that put in place the decision making process. There are not substantial differences concerning the treatment given by the legislation to LMOs in a general sense. The differences are appointed, mainly, in the information that the applicants for authorizations must submit to the regulatory agency. The Resolution has 5 annexes regarding LMOs, which are the base for the technical dossier to be submitted by the applicants to the regulatory body. Three of them are referred to microorganisms and viruses. The first one is aimed at the facilities in which activities involving microorganisms and viruses are undertaken. The second involves activities like research, trial and release of biological agent (LMOs are included). Finally, we have a third one directed to import and export of LMOs (microorganisms and viruses are included).

Those annexes have a little difference concerning the annex 3 of the Cartagena Protocol. This difference is aimed at focusing the elements contained in annex 3 to the case of microorganisms and viruses. Those aspects are the risk group, its capacity of producing some diseases to the man, animals and plants, incubation period, infection ways, prophylaxis measures and treatment, among other.

E. Response to the invitation to the discussion group on risk assessment and risk management of transgenic microorganisms and viruses [#755]

This is my current response to the invitation to the Discussion Group on risk assessment and risk management of transgenic microorganisms and viruses. But, my comment is rather general in nature and may be at least partially relevant to other LMOs.

My apology is that, on account of short notice, I had not enough time for careful draft, and I may have to change some of my comments later.

<How to apply Annex III of the Protocol when assessing the risks of transgenic microorganisms and viruses>

Annex III. Risk Assessment

Objective

1. The objective of risk assessment, under this Protocol, is to identify and evaluate the potential adverse effects of living modified organisms on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account risks to human health.

Comment 1

In my personal view, interpretation of this paragraph is controversial.

1. Conservation of biological diversity: First, I recognize that the term "biological diversity" is value-laden. For example, my backyard with variety of weeds may contain more species than the well conserved garden for conservation of a rare plant species. The latter is surely more important from biodiversity conservation view point. It is not just number of species that count. Second, how we define "conservation"? Environment is constantly changing without human intervention. Rain fall, temperature, humidity, interaction among living organisms, interaction of living organisms with environment etc, they are changing every minutes affecting the life of every organism and hence "biodiversity". You can never conserve biodiversity in the status quo. This problem relates to the point made in this inquiry "difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc." Baseline data of the last two years may not be valid for coming years, even for the next two years in the present drastic climate change.

2. Adverse effects: The term "adverse" is again value-laden. Suppose a land containing toxic metals, where we find unique fauna (biodiversity) of microbes. If the heavy metal is removed by bioremediation, the microbes living on the heavy metals may disappear and unique biodiversity will be destroyed. The bioremediation has adverse effects on the biodiversity unique to the polluted land. If the Annex is interpreted in this way, there is no room for remediation of the polluted soil.

3. The above arguments may seem stupid, but clarifying the above points is vital for this Annex to be used in the real world. In my personal view, it is important to recognize that this paragraph is value-laden and can be variably interpreted depending upon how people value the environment. Objective parameters for measuring the biodiversity may be illusory. The whole responsibility is on the shoulders of the human beings who value the environment. If this interpretation is accepted, it could be most important to agree first on biodiversity and environment that we want for the receiving environment. We should clearly identify living species and environment that we want to conserve or alter after releasing LMOs.

Use of risk assessment

2. Risk assessment is, inter alia, used by competent authorities to make informed decisions regarding living modified organisms.

Comment 2

As indicated below, risk assessment should be conducted regarding LMOs and receiving environment in combination. The term "living modified organisms" in this paragraph should be so interpreted.

General principles

5. Risks associated with living modified organisms or products thereof, namely, processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology, should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment.

Comment 2

1. In my view, this paragraph is the most important paragraph in the Annex. The idea is consistent with the substantial equivalence or comparative safety assessment used in the codex's safety assessment of the food derived from modern biotechnology.

2. However, the phrase, "the non-modified recipients or parental organisms in the likely potential receiving environment", may need further clarification.

3. In the receiving environment, innumerable varieties of organisms beyond our knowledge are present. Just think of soil microbial diversity. They are interacting among themselves and interacting with environment. Soil biodiversity is important for plant growth and indirectly for animals which feed on the plants. We can never know the environment in its entirety. Assessing risk of each of the innumerable interactions of the living organisms is futile and even inappropriate for the risk assessment. One important consideration in environmental risk assessment, in my view, is to assess the organism and environment as a set by using the concept of familiarity1 developed by OECD in early 90's.

4. Codex alimentarius in its consideration of safety assessment of the food derived from modern biotechnology defined conventional counterpart, which is "a related plant variety for which there is experience of establishing safety based on common use as food", which may correspond "the non-modified recipients or parental organisms in the likely potential receiving environment" in Annex III. It is important to note that this provision does not apply if LOM has no conventional counterpart(s).

5. As no two environments are equal, if we transpose the codex conventional counterpart definition onto Annex III, the latter should be interpreted as "a related living organism already present in the receiving environment or in the like environment". We can never know environmental processes in each detail, but we do "know" or are "familiar with" the organism and its interaction with the receiving environment despite of their instability over time. This approach may allow us more focused risk assessment (focusing on the introduced trait).

6. For LMOs obtained by using organisms from other places, the risk assessment should be split into two steps, assessment of the recipient organism as an organism exotic to the receiving place and assessment of genetic modification itself.

7. The following are definitions/explanations of familiarity and substantial equivalence of OECD and codex respectively.

"Familiarity" from Safety considerations for Biotechnology: Scale-Up of Crop Plants (OECD)

- Familiarity is not synonymous with safety; rather it means having enough information to be able to judge the safety of the introduction or to indicate ways of handling risks.

(i) Familiarity with the characteristics of the organism, the trait introduced, the interactions between these, and the intended application.
(ii) Familiarity with the conditions and the environment into which the organisms are intended to be introduced.
(iii) Familiarity with interactions among the organism, the trait and environment.

"Substantial Equivalence" (redefined) from Guideline for the Conduct of Food Safety Assessment of Foods Derived from Modern Biotechnology (Codex Alimentarius)

- 13. The concept of substantial equivalence is a key step in the safety assessment process. However, it is not a safety assessment in itself; rather it represents the starting point which is used to structure the safety assessment of a new food relative to its conventional counterpart. This concept is used to identify similarities and differences between the new food and its conventional counterpart2. It aids in the identification of potential safety and nutritional issues and is considered the most appropriate strategy to date for safety assessment of foods derived from recombinant-DNA plants. The safety assessment carried out in this way does not imply absolute safety of the new product; rather, it focuses on assessing the safety of any identified differences so that the safety of the new product can be considered relative to its conventional counterpart.

Methodology

8. To fulfil its objective, risk assessment entails, as appropriate, the following steps:

(a) An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health;
(b) An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism;
(c) An evaluation of the consequences should these adverse effects be realized;
(d) An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized;
(e) A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks; and
(f) Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment.

Comment 3

General

1. The above provisions are more appropriate for chemicals such as herbicides or insecticides than for living organisms. Differently from the case of chemical pollutants, for living organisms it is often not clear what or what level is adverse to the biodiversity and what is not (particularly in environmental use of microbes).

2. As interpretation of terms “adverse” and “biodiversity to be conserved” depends on each person’s ethical thinking, these provisions are difficult to use in the science-based risk assessment. These terms are more appropriate for risk management.

3. I often noticed that this paragraph is used in isolation without taking paragraph 5 into account. Any living organisms have “adverse” effects on some organisms and “beneficial” effects on other organisms. Any risk assessment should be based on this understanding. In addition, the environment and consequently biodiversity are constant changing for better or for worse without human intervention.

4. It is important to note that these provisions should be used always with reference to paragraph 5.

Points to consider

<Experience in conducting risk assessment of transgenic microorganisms and viruses>

In my knowledge, Japan has not yet approved use of microbial LMOs in environment. I once chaired a committee that evaluates bioremediation trial with non-GM microbes. The site was a land heavily polluted by TCE. The trial revealed many interesting issues. The survival of introduced microbes and level of the pollutant never remain stable; it goes up and down. The data is highly variable depending upon the site of sampling. Rain fall dry heat greatly affected the data. I even asked myself whether the monitoring as a part of the trial ever helped the risk assessment or even it was meaningful. Another problem I experienced was the evaluation of opportunistic pathogen. A promising strain isolated from the soil was found to be a member of a species that contains a strain of opportunistic pathogen. It was finally discarded though it was the indigenous soil microbe.

<Recommendations for preparing risk assessment reports>

1. The Annex III contains paragraphs whose interpretation is quite controversial when it is applied in the real world. It causes litigation uncertainty and blocks potentially useful application of LMOs in the environment.

2. As the member countries are striving to make their regulation in line with the Cartagena protocol, it is important that the risk assessment guidance is realistic.

<Other comments>

1. Receiving environment may need further clarification in relation to ecological niche. Even for fishes living in the free water, they are not occupying everywhere. Ecological definition of receiving environment may be needed.

2. Transgenic pharmaplants could be somehow different from the other LMOs, fish, tree, microorganisms. Some of them are better suited for confined use. If such plants are planted in the field, they could be treated using the "Copy Nature Strategy" (Boulter 1993) cited in pp. 146-148 Plant Biotechnology by Slater, Scott and Fowler (identification of leads, protein purification, artificial-diet bioassay, mammalian toxicity testing, genetic engineering, selection and testing, biosafety).

Best regards,

Hiroshi

TOPIC 4 - RISK ASSESSMENT AND RISK MANAGEMENT OF TRANSGENIC PHARMAPLANTS

Introduction to the topic

by Dr. Robert K. D. Peterson, Montana State University, Bozeman, Montana, USA. E-mail: bpeterson@montana.edu

Pharmaceuticals using genetic engineering have been made through protein expression in bacterial, fungal, and mammalian cell cultures. Biotechnology is currently evolving to produce more complex and diverse pharmaceutical proteins in plants. Using plants offers the promise of large-scale production of therapeutic proteins.

Production of pharmaceutical proteins in plants represents a paradigm shift in the production of pharmaceuticals and biologics, but also in the uses of products formerly limited to food or feed uses. The plant (or food) is not the final pharmaceutical product, just as microbial or yeast pharmaceutical production systems do not represent the final product. Rather, the plant represents just one step in a complex, multi-step pharmaceutical production process. Therefore, most processes in the production of pharmaceuticals will (or should) follow traditional regulatory requirements.

However, the production of these proteins in plants in the environment introduces several unique challenges from regulatory and risk assessment perspectives. Most of these challenges arise from the simple fact that the plants are being produced in the open environment, a unique aspect of pharmaceutical manufacturing. In a field environment, special containment is possible and amenable to strict regulation, but containment is inherently less certain compared with traditional pharmaceutical manufacturing processes. Because of this, questions of potential intra- and inter-species gene flow, allergen exposure to the public, and non-target organism exposure come into play.

Regardless of how specific regulatory activities and responsibilities unfold, the human and ecological risks associated with cultivating these plants in the environment must be assessed using the most robust,

transparent science-based methods available. The established paradigm of risk assessment offers the best approach for assessing these risks.

The risk assessment framework that is practiced most frequently today follows a logical, stepwise process that includes the following procedures: (1) problem formulation, (2) hazard identification, (3) dose-response relationships, (4) exposure assessment, and (5) risk characterization. Hazard and dose are considered in juxtaposition with exposure to determine risk or to determine what additional data are needed to calculate or refine risk estimates. For chemical risk assessments in which a chemical, such as a pesticide, is disseminated into the environment, the exposure assessment step typically is crucial to adequately characterizing risk. Conversely, the problem formulation and hazard identification steps arguably are most important when considering risk from plant-based pharmaceuticals (see journal articles listed below for more information).

The problem formulation step establishes the goals, breadth, and focus of the assessment. Questions that might be addressed during the problem formulation stage include: What is the stressor or activity causing harm?; What are the potential ecological and human health effects?, and; What are the potential exposure scenarios and routes of exposure? The hazard identification step is the act of determining what the hazard is and its ability to cause harm.

The answers to the above questions and actions might be self evident for an environmental contaminant, such as a pesticide, but they are hardly self evident for many plants expressing certain pharmaceutical proteins. For example, what is the stressor in a system in which a potato plant expresses a bovine-specific antigen that will be used as an oral veterinary vaccine? Does the recombinant protein have the ability to cause harm to humans or the environment? Is the potato plant itself hazardous? How do we identify the hazard? Should we conduct a battery of toxicity tests on a large group of non-target species irrespective of our knowledge of the specificity of this antigen or the possibility of exposure? See Shama and Peterson 2008a, b (see below) for more information on potential effects and exposure.

Because of their specificity, lack of toxicity, and therapeutic or disease prevention capabilities, many pharmaceutical proteins that will be produced in plants will challenge our ability to define an environmental hazard. The staggering variety of recombinant proteins that can be expressed by plants demands that the risks associated with them be assessed on a case-by-case basis. A case-by-case analysis fits well within the stepwise nature of risk assessment. Risk assessment is amenable to both quantitative and qualitative approaches. The ability to describe risk qualitatively will probably be important for plant-based pharmaceutical production because of difficulties in establishing a hazard with the highly specific proteins that could be expressed. However, the ability to describe these risks quantitatively is more important for comprehensive societal decision making and communication.

References provided by the author

Shama LM, Peterson RKD (2008a) Assessing Risks of Plant-Based Pharmaceuticals: I. Human Dietary Exposure. Human and Ecological Risk Assessment 14: 179-193. (reprint)

Shama LM, Peterson RKD (2008b) Assessing Risks of Plant-Based Pharmaceuticals: II. Non-Target Organism Exposure. Human and Ecological Risk Assessment 14: 194-204. (reprint)

Peterson RKD, Arntzen CJ (2004) On risk and plant-based biopharmaceuticals. Trends in Biotechnology 22: 64-66. (reprint)

Suggested points for discussion

- How to apply Annex III when assessing the risks of transgenic pharmaplants;

- Experience in conducting risk assessment of transgenic pharmaplants;
- Difficulties in accessing or reviewing baseline information related to the recipient and parental organisms, receiving environment, environmental interaction, etc.;
- Elements necessary to conduct risk assessments of transgenic pharmaplants;
- Issues that are unique to this topic;
- Recommendations for preparing risk assessment reports.

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Interventions

A. Welcome [#743] - posted on 2008-11-09 22:05 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on “Risk assessment and risk management of transgenic pharmaplants”.

The discussions within this group will take place during 10-23 November 2008.

To assist in the discussions, a non-exhaustive list of suggested reading materials, as well as an introduction to the topic, have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum has been made available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

As a participant to the Open-ended Online Expert Forum on Risk Assessment and Risk Management, your contribution is of extreme importance in making this Forum an unprecedented medium of discussion which is a forerunner to the intergovernmental negotiations on the development of guidance material on specific aspects of risk assessment of LMOs.

The CBD Secretariat thanks you for your active participation. Happy discussions!

Best regards,

The Biosafety Division

This is a reply to 743 RE: pharmaplants [#759] - posted on 2008-11-15 06:26 by Prof. Dr. Kazuo Watanabe

This is Kazuo Watanabe, working on LMO risk assessment, management and communication as was introduced in GM trees.

In the case of LMOs-pharmaplants, risk assessment context shall be on the host plant biology as usual as others, and some of potential host species have been well examined in the consensus papers of OECD. Those may be crop species already used in the presently commercialized LMOs-FFP, then, more attention shall be paid for confinement of the gene flow to avoid mixture of the LMOs with non-LMOs.

However, individual nature of the host species well examined in terms of the gene flow.

Allelopathy may be the aspect which shall be carefully observed as the plant produce novel substance which may not be exposed to the environment in the past. With that aspect, plant exudates to soil, interactions with herbivores could be carefully examined owing to the substance produced by the pharmaplants.

However, more importantly, confinement of the LMOs, especially on the gene flow, such as various uses of biological confinement could be one specific aspect for management, besides the general risk assessment issues in order to avoid mis-intaking of the pharma products by the consequence of the gene flow.

Prof. Dr. Kazuo Watanabe

This is a reply to 743 RE: Welcome [#805] - posted on 2008-11-26 14:41 by Michael Schechtman

My name is Michael Schechtman and I work for the United States Department of Agriculture. I have been following the conversations in this forum, and I would like to thank all of those who have contributed. I, along with the three other experts nominated to participate in this forum by the United States Government, consider this to be an important, lively and productive discussion. The risk assessment and risk management of new and novel applications of technology is an important consideration and I thank the Parties and the Secretariat for providing this forum for the exchange of views and information. These comments are a general response to all the discussion threads.

In the United States, we have more than twenty years of experience in the risk assessment and risk management of LMOs – for both experimental use and large scale release into the environment. Based on this experience, we are in agreement with the conclusion of the Norway-Canada Risk Assessment Workshop (June 4-6, 2007). Existing guidance should be adequate to provide risk assessment methodologies for analysis of the relatively new applications of biotechnology referenced in this forum.

There are several internationally developed guidance documents related to risk assessments of LMOs that can be used to evaluate the potential impacts on conservation and sustainable use of biodiversity, including Annex III of the Protocol which provides an excellent outline of the general principles that are applicable to the risk assessment of LMOs. Another prominent example is the OECD "Recombinant DNA Safety Considerations," the so-called "Blue Book". These and other guidelines generally agree that LMO risk assessment should focus on a few basic considerations and their interactions: the organism that has been modified (its biology, lifecycle, level of domestication, and sexual compatibility with wild

species, etc.); the trait that has been introduced (its effect on fitness, the nature of the gene/protein, the origin of the transgene etc.); and finally the receiving environment (is the environment managed or unmanaged, are there protected organisms that might be impacted, etc).

Although risk assessment and risk management can be thought of as separate processes, it is usually acknowledged that risk assessment is iterative, and assessments should take into account risk management measures that may be applied to limit the potential impacts of an LMO on the environment. Most guidance documents also agree that risk assessment should be done on a case-by-case basis and that the amount of information required to make a decision will vary depending on the nature of the LMO; its intended use and the receiving environment – familiar organisms with well-known traits intended for release into highly managed environments are likely to require less information for decision making than organisms that are less familiar that are intended to be used in new ways in highly unmanaged environments.

It is important also to remember that risk assessment and decision making regarding LMOs should not be considered in a vacuum. Other practices and the appropriate context for impacts on biodiversity (in agriculture, forestry, fisheries, etc.) should be factored into the assessment. The impacts of LMOs on the conservation and sustainable use of biodiversity should be considered in comparison to their non-transgenic counterparts.

Finally, there is the issue of uncertainty, which is particularly relevant to this forum. New or novel LMOs have more uncertainty regarding their environmental impacts than LMOs that have been in use and for which there is significant national or international experience. This is one reason for allowing experimental releases, to collect data to address this uncertainty. In scientific analyses, absolute certainty is impossible, but existing guidance also provides mechanisms for dealing with uncertainty. From Annex III, "Where there is uncertainty regarding level of risk, it may be addressed by requesting further information… implementing appropriate risk management strategies… or monitoring the [LMO] in the receiving environment." However, it is also important for regulatory officials to have a clear understanding of exactly how new data would be used in a risk assessment prior to requiring such data.

Below you will see links to U.S. regulatory websites and references that may be useful including some to policies and decisions dealing with some of the novel applications considered on this forum. I can also provide contacts and information from U.S. regulatory agencies. U.S. regulatory decisions should be available through the Biosafety Clearing House or links on the U.S. regulatory website. Once again, thanks to all of the participants for an informative discussion and to the Parties and the Secretariat for providing the forum and the opportunity to participate.

OECD "Blue Book" – Recombinant DNA Safety Considerations

http://www.oecd.org/LongAbstract/0,3425,en_2649_34537_40986856_1_1_1_1,00.html

Other Relevant OECD Biosafety Documents (BioTrack):

http://www.oecd.org/findDocument/0,3354,en_2649_34385_1_1_1_1_1,00.html

U.S. Regulatory Agencies Unified Biotechnology Website

http://usbiotechreg.nbii.gov/

USDA Guidance for pharmaceutical plant field trials

http://www.aphis.usda.gov/brs/pdf/Pharma_Guidance.pdf

USDA Environmental Analysis and Decision documents for pharmaceutical crops

http://www.aphis.usda.gov/brs/ph_permits.html

USDA Environmental Assessments for non-pharmaceuticals (including trees)

http://www.aphis.usda.gov/brs/biotech_ea_permits.html

Canada -U.S. 2001 Bilateral Agreement on Agricultural Biotechnology Appendix II: Environmental Characterization Data for Transgenic Plants Intended for Unconfined Release

http://www.aphis.usda.gov/brs/canadian/appenannex2e.pdf

B. Transplastomic pharmaplants and related risk assessment issues [#794] - posted on 2008-11-23 16:16 by David Quist

I wanted to take the opportunity to discuss what seems to be important consideration in the risk assessment of some—perhaps in time the majority—of pharmaplants: The use of chloroplast genetic engineering. The use of transplastomic plants for drug production represents a departure from more "traditional" nuclear genome engineering and may raise some unique considerations for risk assessment. While some of these features are not unique to pharmaplants per se, the nature of the target and marker transgenic proteins as bioactive macromolecules deserves particular attention.

Some relevant examples:

HGT potential

Chloroplasts are transformed via homologous recombination, typically via particle bombardment, and utilize bacterial-like border sequences to facilitate site-specific integration of heterologous cassettes (given that chloroplasts genomes former Cyanobacteria). Whether this would alter the transformation frequency of horizontal gene transfer to these microbes in the environment may be important in some cases.

High(er) concentrations of heterologous proteins

Transplastomic plants have been reported to achieve protein expression rates of up to 45% total soluble protein (TSP) of the target protein and 10% TSP of marker genes. The implication of the potential metabolic cost, and hence fitness to the recipient host, along with the impact of greater concentrations of bioactive proteins in the environment may garner consideration in specific uses. The prudence of limiting marker genes in the environment, particularly with antibiotic resistance genes, where possible has been roundly advocated and should follow with strategies to minimize their use in transplastomic plants.

Consistency of maternal inheritance

One widely touted benefit of transplastomic plants is may limit pollen transfer of transgenic sequences, as chloroplast genomes are only maternally inherited (though we all know too well in biology there are few universals!). However, the "leakiness" of this system has been experimentally show to be often variable, and often species dependent. Therefore an assessment of this "leakiness" potential may be warranted in some cases.

RNA editing, post-translational modification, and affinity tag

Related changes in primary and secondary structures of transgenic protein expression

There is evidence that the complex RNA editing of chloroplast transcripts are critical for faithful expression, and translation of unedited exogenous messenger RNAs in transplastomic cassettes could lead to functionally defective proteins. Beyond these transcriptional differences, post-translational modifications are often quite different depending on host. Plants particularly are known to add that may alter it allergenicity (addition of fucose and xylose N-linked glycans) or desired functionality or stability (due to folding or structural differences), all would need to be clarified through validated methods. Lastly the use of affinity tags, such as his or FLAG epitope tags used to facilitate efficient protein recovery and purification from the plant require changes in protein primary structure. A molecular characterization of the insertion site, along with primary and secondary structural features of the target protein and related to potential functional changes, may be necessary for some classes of protein or production systems.

Co-transfer of heterologous integration cassettes to the nucleus

Certain transformation methods, notably Agrobacterium-mediated gene transfer and particle bombardment (the two most common means of transformation) putatively co-transfer integration cassettes into the nucleus in some cases. This represents a distinct regulatory challenge that can be best addressed through localization studies in each transformation event under assessment.

Transgene stability

The maintenance of homoplasmy among the thousands of copies of chloroplast genomes represents one of the big challenges for stable expression of chloroplast-transformed transgenes. Transgene stability may need to be demonstrated, in specific cases, for regulatory approval.

The above scenarios represent some of the known uncertainties surrounding the use of transplastomic plants for the expression of heterologous DNA. As this method is becoming widely used in the production of pharmaplants, well formed questions and validated research methodologies can strengthen the scientific quality of assessments where chloroplast engineering may bring new risk scenarios.

-David Quist

This is a reply to 794 RE: Transplastomic pharmaplants and related risk assessment issues [#834] - posted on 2008-11-29 18:44 by Jack Heinemann

I would like to add to Dr. Quist's comments with regard to chloroplast engineering, with the associated potential use for containment, and Dr. Tappeser's comments about the need for effective containment of transgenes. All references may be found here: ftp://ftp.fao.org/ag/cgrfa/bsp/bsp35r1e.pdf

Neither the US National Academy of Science nor a recent UN FAO report on transgene flow found it realistic, even with the use of hypothetical sterilization technologies, to expect that technology will be sufficient to stop transgene flow. Possibly no combination of technology and human management may be sufficient either. Therefore, for the foreseeable future, only contained laboratories can serve to manage the risks from GMOs that may cause unacceptable harm if the transgene were to escape.

This is a reply to 834 RE: Transplastomic pharmaplants and related risk assessment issues [#838] - posted on 2008-11-30 15:47 by Luther Val Giddings

I'd like to offer some comments on both 794 and 834.

In re 794, Dr. Quist makes some interesting points, but fails to acknowledge some overarching facts of salient importance. There are no uncertainties or safety issues that the current processes of risk assessment and management are incapable of dealing with; indeed, a number of them have been dealt with in the context of transgenic plants not intended for use in pharmaceutical production from the very beginning, e.g., the issues of stability in construct inheritance, potential fitness impacts of the transgenic

modification, potential for horizontal transfer, species specific impacts of various sorts, and so on. Nothing here is novel or unfamiliar.

A more fundamental issue not acknowledged either in posts 794 or 834 is that of hazard identification – both postings seem to assume a necessarily higher level of intrinsic hazard from PMP plants than from other transgenic (or conventional) plants. This is not a reliable assumption, as long experience has shown with conventional plants from which pharmaceuticals have been derived (vincristine and vinblastine from Madagascar periwinkle; salicylic acid from Salix spp., Vitamin E from soya or C from citrus, etc.) and on to components from mother's milk in modern transgenic plants, such as lactoferrin, in rice. It would not be a good and reasonable investment of resources, nor a scientifically defensible approach to risk assessment and management, to treat all PMP plants as if they are potentially highly hazardous, and regulators and policy makers should not lose sight of such facts.

Even with plants making pharmaceuticals that are demonstrably safe, however, market disruptions can occur if they wind up where not desired. Food companies are concerned about their brands which may suffer if unapproved materials (safe or not) are found in them, rendering them "adulterated" under law. For this reason many PMP companies are trying to work with non food plants, but even those using food plants are devoting unprecedented attention to identity preservation, with considerable isolation distances, dedicated machinery, and other methods of containment. No company would rely solely on biological containment, as many biological measures can be, under certain circumstances, less than absolute, as noted in 834. This is why developers of PMP routinely rely on a defence-in-depth approach using multiple different methods intended to contain PMP materials and keep them out of places they are not wanted.

It is also the case that for the foreseeable future regulatory agencies will continue to treat each and every PMP field trial request with focused, case-by-case attention to ensure materials are properly handled without surprises.

But in all of these cases, the potential for PMP caused impacts on biodiversity are effectively indistinguishable from zero. While agriculture itself has huge impacts on biodiversity (primarily through the loss of native lands converted to agricultural production) the areas involved in PMP production will be, at best, miniscule by comparison to the land devoted to agriculture in general. The extraordinary added value of PMP plants will ensure high levels of containment and special handling likely to mitigate or eliminate any significant hazard to biodiversity. On any list of the top threats to biodiversity, no serious scholar of biodiversity would place PMP plants. There are many more real and present dangers.

C. Unique aspects of pharmaplants [#817] - posted on 2008-11-28 10:02 by Beatrix Tappeser

Pharmaplants are of special concern when possible environmental and biodiversity aspects are considered. As acknowledged in the Norway –Canada Workshop 2007 pharmaplants may pose unique risks to the environment e.g. because of the novelty of the pharma compound itself or the novelty of the exposure to the environment. Multiple interactions with herbivores, their predators, pollinators and any other organism being part of the food web and the interacting biocenosis network are to be taken into consideration. Distribution and spread via seeds, pollen or with the help of vegetative proliferation has to be prevented. Current risk assessment using concepts like substantial equivalence or familiarity as starting points are not suited for an environ-mental assessment of pharmaplants. There is the need of developing physical containment concepts which really live up to the expectations of a fully reliable containment. Out of a nature protection perspective this is somehow a prerequisite for the use of pharmaplants as production facilities for drugs or other potent substances.

This is a reply to 817 RE: Unique aspects of pharmaplants [#832] - posted on 2008-11-29 18:15 by Jack Heinemann

I agree with Beatrix Tappeser's comments on pharmaplants. However, in the rush to put such products to regulators there may be the temptation to argue that without an appropriate conventional comparator upon which to apply "the history of safe use", we should apply comparators that are even less suited to the purpose of hazard identification. This is, in my opinion, what happened in at least some regulatory approvals of high lysine corn LY038. This product was acknowledged by all to be modified to be not substantially equivalent to any kind of corn or vegetable in existence. In the case of that corn, the various hazards were dismissed by what I consider to be some regulators' far-fetched comparisons to red meat, button mushrooms and chicken eggs.

The problem with this is two-fold. First, even if one were to accept that hazards from the modification of a plant can be identified and dismissed based on comparisons to similar compounds in other kinds of foods, there remains the problem that the plant-derived hazard may be prepared differently and consumed in different amounts. Second, this approach equates the overall safety and value of a food with each of its parts. Some hazards in milk and meat are balanced by the overall nutritional benefits of these foods in the diets of many people. That does not make each component in these products safe at comparable concentrations in other plants nor does it justify moving a potential hazard into a food product that has historically been free of this potential hazard.

The use of historical literature to define acceptable ranges of compounds in a species must be abandoned in favour of descriptions that emphasise the overall physiological balance in the test and comparator at the same time and location. It is dubious to argue, for example, that because some corn plants grown somewhere in the 1920s may have had sodium levels 5 times that of the proper comparator grown in 2008 then significantly higher sodium levels in the GM plant is also justified. This is because we don't know anything about how the 1920s plant may have compensated for this sodium or even if it resembled a proper corn plant.

It could be argued that pharma is a more blatantly hazardous modification and therefore this temptation, that has seduced regulators in the past, will not be so powerful in the future. However, this argument is speculative as developers cleverly undermine regulators' worries about just how dangerous a pharma-protein is (e.g., because of claims that it will be digested etc.). And as developers make drugs based on multiple components raised in different plants and which they will argue only have a pharma property when combined through industrial process highly unlikely to exist in nature. None of these arguments are of scientific origin as much as they will be designed to reassure.

Thus I would argue that more attention needs to be paid to the scientific description of comparators with every effort placed on making this definition more stringent and meaningful than it has been in the past. Doing this for pharma can have retrospective benefits for first generation GM products.

D. General matters in transgenic plants [#782] posted on 2008-11-21 05:34 by Yasuhiro Yogo

In case natural plants cross-compatible with LMO exist, non-LM crop should be used not only no-effect standard but also effect standard of introgression. The reason is as follows. Crop was developed from natural plants, for human needs, such as stable yield and good taste (quality). In other words, crop lost the several properties of weeds (weediness). Once crop genes, even in none-LMO, make introgression to the natural plants, these natural plants may lose weediness or ability for survival. This impact should be taken into account for risk assessment of transgenic plants.

Gene introgression via seed should be focused as well as via pollen. This introgression may cause spatially (seed dispersion) and temporally (seed bank). When LMO voluntarily invade into natural circumstances, we mainly focus on competitive advantage. However, seed longevity also important, since its adverse effects on the biodiversity remains in long term. Therefore plants which have strong potential to form seed bank should not be appropriate as host for LMO.

Just for your information, I will add the domestic rules on Cartagena Protocol in Japan in Library site soon.

This is a reply to 782 Domestic law and regulations on Cartagena Law in Japan [#788] - posted on 2008-11-22 01:41 by Yasuhiro Yogo

Please find following URL on the domestic law and regulations on Cartagena Law in Japan.

The list of approved LMOs is also available with Type 1 use (open field) regulation and the risk assessment.

Approved LMOs in are totally 136 until mid. October, 19 (2008), 29 (2007), 31 (2006), 33 (2005), and 24 (2004). Most of them are transgenic crop in Type 1 use (open field), and the major traits are herbicide (glyphosate, glufosinate) resistant and the resistant to insects with the protein from BT.

URL: http://www.bch.biodic.go.jp/english/law.html

Best regards,

Y.Yogo

E. Definition of pharmaplants [#780] - posted on 2008-11-21 05:32 by Yasuhiro Yogo

Based on "Pharmaplants Session" in REPORT OF THE CANADA-NORWAY EXPERT WORKSHOP ON RISK ASSESSMENT FOR EMERGING APPLICATION OF LIVING MODIFIED ORGANISUMS (UNEP/CBD/BS/COP-MOP/4INF/13), pharmaplants include the plants which produce therapeutics, diagnostics and vaccines as traits. They do not include industrials and nutraceuticals. In Japan, we developed peptide immunotherapy for allergic diseases using a rice-based edible (needle-free) vaccine, targeting what we call, "cedar pollen allergy (see below, I will put them in Library site soon)", and it is involved in pharmaplants.

I agree that we had better focus on pharmaplants based on the above definition in this session. However, we should bear in mind the other plants, which produce organic substances for the other use than pharmaceuticals, since they also have potential to affect on the biodiversity as well as the pharmaplants.

Literature¬

Nochi, T., et al. .″ Rice-based mucosal vaccine as a global strategy for cold-chain- and needle-free vaccination. Proc Natl Acad Sci U S A. 104:10986-91, 2007.

Hiroi, T. and″ Takaiwa, F. Peptide immunotherapy for allergic diseases using a rice-based edible vaccine, Curr. Opin. Allergy. Clin. Immunol., 6: 455-460, 2006.

″Takagi, H., et al. A rice-based edible vaccine expressing multiple T cell epitopes induces oral tolerance for inhibition of Th2-mediated IgE responses. Proc. Natl. Acad. Sci. USA. 102: 17525-17530, 2005.

In case of pharmaplants, there are two growth condition, open field and glasshouse (closed condition), depending on cropping size and trait, as Leticia Pastor Chirino pointed out. I propose that we focus on open field. Because the assessment items in closed condition are limited within disposal and pollen dispersion in view point of biodiversity.

This is a reply to 780 Literature on transgenic pharmaplants for cedar pollen allergy in Japan [#787] - posted on 2008-11-22 01:19 by Yasuhiro Yogo

Just for your information, please find the URL of the literature on pharmaplants (peptide immunotherapy for cedar pollen allergy) in Japan. The following manuscripts are two of three ones in the previous mail.

1) Nochi, T., et al. . Rice-based mucosal vaccine as a global strategy for cold-chain- and needle-free vaccination. Proc Natl Acad Sci U S A. 104:10986-91, 2007.

=>URL:http://www.pnas.org/content/102/48/17525.abstract

2) Takagi, H., et al. A rice-based edible vaccine expressing multiple T cell epitopes induces oral tolerance for inhibition of Th2-mediated IgE responses. Proc. Natl. Acad. Sci. USA. 102: 17525-17530, 2005.

=>URL: http://www.pnas.org/content/102/48/17525.abstract

Best regards,

Y.Yogo

F. Assess items which should be newly evaluated in pharmaplants [#781] - posted on 2008-11-21 05:33 by Yasuhiro Yogo

Traits (transgenic genes) in pharmaplants inevitably modify the metabolism. Then the following points may be raised as ad hoc assessment items.

a) Productivity of harmful substances full life cycle and each part of plants, including seeds and fruits.
b) Adverse effects on the predators such as mammals (except for human), birds, earthworm, and the other small animals
c) Productivity of unexpected harmful substances in natural plants cross-compatible with LMO, after transgenic genes were transferred to the plants

Gene expression was regulated in limited part of plants or full body by each promoter. And the traits, crop and environment are different among events and countries. Therefore case by case approach is needed to consider the above points.

In addition, we should bear in mind about adverse effects of volatile metabolites on natural plants, since some metabolites may have high vapour pressure, such as aromatherapy.

As far as I understand, we will discuss on adverse effects on biodiversity of pharmaplants here. Therefore, occupational exposure and oral toxicity for human should not be discussed, or at least separately discussed. On the other hand, oral/Inhalation toxicity for natural living organisms should be carefully discussed, since some metabolites derived from introduced gene may cause unexpected toxicity to natural living organisms.

G. The first address and the mission of the session of transgenic pharmaplants [#779] - posted on 2008-11-21 05:30 by Yasuhiro Yogo

I am Yasuhiro YOGO, National Institute for Agro-Environmental Sciences, Japan. I have been major in weed science, and now in pesticide science.

I put comments (threads) as follows. I hope that the following comments will contribute active debate in this Online Expert Forum. I divided into four threads including this thread.

1. Mission of this session

I would like to propose that outline of the demands should be discussed as a first step, although trait, host plant, growing condition will be case by case. Following threads will help to start discussion about the above matter.

H. Risk assessment and risk management of pharmaplants in Cuba [#774] - posted on 2008-11-19 17:17 by Leticia Pastor Chirino

My name is Leticia Pastor Chirino, I am the Head of the Authorization Department of the National Center for Biosafety in Cuba. In the case of Cuba at this moment only one research involving Pharmaplants´ development has been authorized, this research is still in an early stage, with a small number of plants under confinement conditions (Green House).

The risk assessment and the risk management process in this case is not different from other processes but in our country the activities involving the obtaining of Pharmaplants is always done under confinement conditions and its use will be limited only for the obtaining of pharma products. The rest of the plants should be destroyed avoiding its use with other objectives.

I. Available Examples of Risk Assessments for Pharmaplants [#763] - posted on 2008-11-16 11:36 by Dr Ossama Abdel-kawy

A limited number of pharmaplants have been grown in field trials under strict conditions to minimize their interactions with the environment. These trials have taken place for over 10 years in various locations within Canada, the USA, and the European Union (EU). When reviewing applications for these field trials, regulators in these countries have focussed on the following general risk assessment criteria:

- the identity and origin of the pharmaplant;
- the properties of the novel gene and gene product(s);
- anticipated or known effects on the environment;
- description of the proposed trial site, particularly any presence of endangered species in the trial site area
- potential impacts on human and animal health resulting from the environmental release;
- the experimental protocol
- measures that will be taken to ensure reproductive isolation of the trial plants, trial site surveillance, and restrictions of post-harvest land use as well as proper record keeping, safe handling, storage and disposal of plant material;
- Contingency plans, should the pharmaplant be released outside of its authorized area, or unintentionally enter the food or feed supply chains.

In Canada, the CFIA oversees confined field trials of plants with novel traits according to the general risk assessment criteria outlined in "Directive 2000-07: Conducting Confined Research Field Trials of Plants With Novel Traits in Canada". However, the CFIA has also adopted stricter risk mitigation measures for confined field trials of pharmaplants. These are outlined in the "Interim Amendment to Directive 2000-07 for Confined Research Field Trials of PNTs for Plant Molecular Farming" and include, among other things, increased reproductive isolation requirements.

In the USA, field testing research using pharmaplants requires a full APHIS permit. These permits require more detailed information than what is normally required for standard notifications. Decision summaries for all release permits are publicly available online.

Various member countries of the EU have also authorized confined field tests for pharmaplants. In France, field trials of corn expressing a gastric lipase were authorized in 2000, with trials of corn expressing monoclonal antibodies following in 2005. Applications for these trials and summaries of the

risk assessments performed by the French authorities can be found online (French only). In Germany, field trials of potatoes expressing a de-toxified cholera toxin subunit and potatoes expressing viral coat proteins from rabbit haemorrhagic disease were authorized in 2006. Notification reports for all confined field trials in the EU are available on the website of the Joint Research Centre of the European Commission.

While this technology is rapidly moving towards commercialization, there are currently no known authorizations for large-scale releases of pharmaplants into the environment. However, it is anticipated that this will change in the near future as developers have expressed interest in submitting applications for non-research releases within 1 to 3 years.

TOPIC 5 - RISK ASSESSMENT AND RISK MANAGEMENT OF LMOS WITH STACKED GENES OR TRAITS

Introduction to the topic

Gene stacking (also known as gene pyramiding) is the process of combining two or more transgenes into an organism.

There are many different ways for obtaining a stacked event, traditional breeding by crossing two genetically modified events being, at the moment, the most common method for stacking genes in commercial genetically modified crops. Other methods include, for instance, co-transformation, re-transformation and multi-gene cassettes. Examples of stacked LMOs include MON863 x MON810 x NK603 (double cross breeding), Bt-11 (cassette with multiple genes) and Bt176 (co-transformation).

Detection methods of stacked genes should be precise enough to allow for the identification of each transgene. Monitoring of stacked organisms deserves particular attention because of possible segregation of the transgenes.

According to the Protocol, risk assessment of LMOs must be carried out on a case-by-case basis; as such each event containing stacked genes/traits must undergo risk assessment.

Suggested points for discussion

- In addition to the steps taken when assessing the safety of single-transgene events, which elements should be considered when conducting risk assessments of LMOs with stacked genes?
- How to assess potential interactions and synergism resulting from the presence of multiple transgenes? (e.g., altered toxicity to target or non-target organisms and any consequential impact on the development of resistance in target organisms, altered fitness of the genetically modified organisms acquiring the transgene combination through gene flow, etc.)
- Further issues that are unique to this topic;
- Recommendations for preparing risk assessment reports of LMOs with stacked genes or traits.

List of threads and number of replies

Thread title	*Number of replies*
A. Welcome to the second round of discussions	0

B. Suggestions for improving the risk assessment of LMOs with stacked events	2
C. Stacked genes	2
D. Risk assessment and risk management of LMOs with stacked genes or traits	0
E. Risk assessment and risk management of LMOs with stacked genes or traits	0

Interventions

A. Welcome to the second round of discussions [#844] - posted on 2008-12-01 00:56 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Risk assessment and risk management of LMOs with stacked genes or traits".

The discussions within this group will take place from 1 to 14 December 2008.

To assist in the discussions, the following is a non-exhaustive list of suggested points for discussion:

1. In addition to the steps taken when assessing the safety of single-transgene events, which elements should be considered when conducting risk assessments of LMOs with stacked genes?

2. How to assess potential interactions and synergism resulting from the presence of multiple transgenes? (e.g., altered toxicity to target or non-target organisms and any consequential impact on the development of resistance in target organisms, altered fitness of the genetically modified organisms acquiring the transgene combination through gene flow, etc.)

3. Further issues that are unique to this topic;

4. Recommendations for preparing risk assessment reports of LMOs with stacked genes or traits.

Also, an introduction to the topic, as well as a non-exhaustive list of suggested reading materials have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum is available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

The CBD Secretariat thanks you for your active participation. Happy discussions!

The Biosafety Division

B. Suggestions for improving the risk assessment of LMOs with stacked events [#860] - posted on 2008-12-10 09:44 by Helmut Gaugitsch

In Austria we have recently undertaken a project on the risk assessment of LMO products with stacked events. In this context we have identified some shortcomings concerning the approach to and the available

guidance for the assessment of such applications. Most of the controversy is about requirements in addition to the data submitted for the parental LMO events.

Our study identifies open questions and the need for further clarification and research concerning the risk assessment of stacked events (Spök et al. 2007).

Some of the key issues identified appear to be less controversial or not controversial at all:

- Risk assessment of stacked events can draw on the assessment of parental LMO plants and should consider the results of such assessments.
- Requirement for a molecular characterisation in order to confirm the preservation of the inserted traits and to compare the expression of transgenes between parental LMO events and the stacked event.
- Comparative analysis of the stacked event including a standard set of compositional and agronomic parameters.
- Need to consider any potential interaction of combined traits in the stacked events.

On the other hand, some issues are debated more intensively and require further clarification, discussion and research:

- Can the methods used for molecular characterisation be considered sufficiently precise to achieve demonstration of identity with parental events?
- Should the parental LMO events be included in the comparative analysis of plant compounds, agronomic traits, and expression of the transgenes along other comparator lines?
- How should the potential interaction of traits be assessed and at what levels (genetic, protein, metabolic)?
- What would trigger the need to conduct whole food toxicity studies with the stacked event?

At present the latter questions are neither appropriately addressed in the risk assessment dossiers nor covered adequately by available guidance documents. The Guidance Document available at the EU level is the EFSA guidance document on the risk assessment of stacked events (EFSA 2007). According to this document a case-by-case flexibility as to which requirements listed for the risk assessment of single event LMOs would apply for the assessment of stacked events is necessary. The assessment should focus on issues related to

- Stability
- Expression of traits
- Potential synergistic or antagonistic effects resulting from the combination of traits.

Specifically the last issue presents challenges regarding experimental investigation and appropriate methodology. In current practice such assessments only rely on the theoretical discussion of the lack of probability of interactive effects in stacked events , although there is evidence from the published literature for such interactive (synergistic, antagonistic) effects, for example of plant-produced proteins and toxins such as Bt toxins (Spök et al. 2008). From a precautionary point of view, it is necessary to conduct specific assessments with the whole stacked event LMO plant in order to test for potential interactive effects of the traits on the molecular, the protein or the metabolic level. The parental, single event LMOs should be used as comparators in these tests in addition to a non-LMO comparator.

In notifications of stacked events introduced in the EU the stacked event itself is only assessed experimentally in the comparative analysis of plant compounds, the characterization of agronomic traits and the expression of the transgenic traits. Controversy exists with regard to the need for further whole plant studies for food safety and environmental aspects (for details see Spök et al. 2007).

In the context of the large numbers of combinations of different proteins, toxins or other gene products which can be obtained by gene stacking, the general aim should be to assess potential effects of combined

traits in stacked events in a case-by-case assessment under realistic environmental conditions. This objective should be supported by detailed and scientifically robust guidance.

EFSA (2007). Guidance document of the Scientific Panel on genetically modified organisms for the risk assessment of genetically modified plants containing stacked transformation events. Adopted on 16 May 2007. The EFSA Journal 512, 1-5.

Spök A., Dolezel M., Eckerstorfer M., Freigassner M., Gaugitsch H., Heissenberger A., Karner S., Klade M., Proksch M., Schneider L., Treiber F. & M. Uhl (2008a). Assessment of toxic and ecotoxic properties of novel proteins in GMOs. Bundesministerium für Gesundheit, Familie und Jugend, Forschungsberichte der Sektion IV, Band 1/2008.

Spök A., Eckerstorfer M., Heissenberger A. & H. Gaugitsch (2007). Risk Assessment of stacked events. Untersuchungen zur Risikoabschätzung von „stacked events". Bundesministerium für Gesundheit, Familie und Jugend, Forschungsberichte der Sektion IV, Band 2/2007.

This is a reply to 860 RE: Suggestions for improving the risk assessment of LMOs with stacked events [#883] - posted on 2008-12-18 18:36 by Prof. Dr. Kazuo Watanabe

This is more response to the previous comments.

The evaluation of the stacked lines shall be principally with the RA for the original LMOs.

But again, the reproductive nature and genetics of the species, especially plant species with outcrossing and heterozygous status of the parental lines could have a large segregation besides the transgene per se. With the new genotype together with the transgene, assessments shall be made accordingly to if transgene x new background genotype change could alter the traits including stability. My comments may correspond mostly with the Dr. Helmut, but my point could be more on plant breeding with outcrossing species. While it is true that focus shall be made on the behaviour of transgene in the stacked line, always genetic segregation is the major basis of plant breeding, attention shall be made on the trait performance in the progeny line (stacked line).

Regards,

This is a reply to 860 RE: Suggestions for improving the risk assessment of LMOs with stacked events [#902] - posted on 2008-12-19 15:51 by Ricarda Steinbrecher

As already pointed out by others on this discussion group, there are some key issues that are mostly agreed upon and then again there are other key issues that still require further discussion and probing.

I want to add some arguments to the second group of key issues.

There has been a tendency to focus on trait-specific risk assessment and not paying sufficient attention to the assessment of unintended changes (both DNA level as well as metabolic pathway level) or looking for unpredicted or unpredictable effects. This includes for example the assessment of transformation induced mutations (both genome-wide mutations as well as insert site specific mutations), which have substantial potential for giving rise to unpredicted effects and where further research is still urgently required (Wilson et al. 2006).

Concerning gene stacking I regard it as crucial to not only look at the traits as a matter of adding them up individually, but also to assess what mutational burdens have been introduced through/by the stacking process (whether this is by additional transformation or cross breeding of previous GM events).

Furthermore, toxicology has taught us, that if consuming substance A is safe when eaten on its own and substance B is safe when eaten on its own, a completely different scenario may arise when substance A and B are consumed together – they may indeed be toxic together. Whilst such synergistic effects are widely recognised now in toxicology and even made use of in vaccines and chemotherapy when utilising adjuvants, we seem to find it difficult to apply the same standards to genetically engineered organisms (LMOs).

Until otherwise proven safe, our starting point for risk assessment of stacked genes should be treating the particular LMO as a brand new LMO and carry out risk assessment accordingly, including metabolic studies, field trials and feeding trials. Of course, the assessments of the parental lines are going to be of use in this process, but only as a starting point.

With regards to the stacking of multiple insecticidal genes, there is also the question of cumulative affects as well as increased or new allergenicity, for both ingestion as well as inhalation or touch.

Literature cited:

Wilson AK, Latham JR & Steinbrecher RA (2006). Transformation-induced mutations in transgenic plants: Analysis and biosafety implications. Biotechnology and Genetic Engineering Reviews 23: 209-234.

C. stacked genes [#875] - posted on 2008-12-16 04:27 by Ph.D. Lúcia de Souza

It is useful to consider the question of stacked genes in context. Traditional breeding methods often introduce genes from species that do not normally cross in nature. These methods, in effect, introduce hundreds, or even thousands, of stacked genes. With these methods, we cannot assess the safety of the stacked genes, and the interaction of these genes with each other, on a gene-by-gene basis. There are too many genes involved, and for most of the genes, their functions, and their interactions with other genes are unknown. However, plant breeders assess these stacked gene introductions and their interactions on a more global basis by testing plant varieties for productivity, resistance to abiotic and biotic stresses and quality in many environments on a trait or product basis, i.e. the safety and productivity of a plant variety, whether transgenic or not, is typically tested in multiple environments over multiple generations, genetic backgrounds and years. In cases where biochemical pathways or specific analyzable characteristics may be known to be adversely affected, these characteristics are analyzed. Any detrimental characteristics are eliminated during the breeding process when commercial varieties are developed. Due to the rigorous testing in plant breeding there have only been a few documented cases of safety hazards in crop plants. As a result crops traditionally bred have provided a safe food supply for a century and are not subjected to risk assessment by most countries, These methods of assessment have been or are applied to transgenic crops, and achieve the same level of safety.

However, LMOs are subjected to additional assessments and therefore, those that have been approved for commercial release using the risk assessment framework set forth in documents such as Annex III of the Cartagena Protocol, achieve an even higher level of safety that traditionally bred varieties. This conclusion is supported in a publication by the European Commission in 2001, reporting the results of 81 Research Projects performed over 15 years:

“Research on the GM plants and derived products so far developed, following usual risk assessment procedures, has not shown any new risks to human health or the environment, beyond the usual uncertainties of conventional plant breeding. Indeed, the use of more precise technology and the greater regulatory scrutiny probably make them safer than conventional plants and foods…”

The existing framework for risk assessment can be readily applied to the assessment of stacked genes introduced into crop varieties. The assessment of these genes provides the advantage that they are well characterized in comparison to those introduced by traditional breeding. For clarity, we are using the term "stacked" in this posting to mean combinations of transgenes achieved either by the cross-breeding of individual LMO lines or the direct introduction of multiple genes via transformation. In both situations, the sequences and functions of the introduced genes are known, and the interactions between the introduced genes can be better predicted. Where knowledge of these genes and their interactions is not sufficient, gaps can be filled prior to commercial release by conducting the appropriate tests in field trials. This increased information enables us to do a risk assessment with these stacked genes, which we could not do with traditionally bred varieties. The additional risk assessment goes beyond the already safe and proven system now used for plant breeding.

Annex III of the Cartagena Protocol provides a robust framework for risk assessment. It provides a means by which LMOs can be assessed for safety, whether they contain a single or multiple transgenes, and whether multiple transgenes have been incorporated by traditional breeding methods or by transformation via a single vector. It should be pointed out that this framework applies to environmental effects and impacts, and does not include questions of food safety, which are not covered under the Protocol.

Adequate guidance in the risk assessment of stacked genes has been published by various regulatory agencies. Examples are given in the supplementary readings posted by the BCH in connection with this online forum. PRRI considers these guidance documents as good sources of further detail regarding risk assessment within the framework of Annex III. Regulatory decision documents covering the risk assessment of various stacked events or varieties can also serve as examples for conducting risk assessment with stacked genes. These documents are available on the web sites of many regulatory agencies.

PRRI has published a guide to conducting risk assessments that is also consistent with Annex III, and which can be applied to the assessment of stacked genes. This guide takes a step-by-step approach to risk assessment, and can be applied to any number of genes that may be present in a specific LMO. This guide can be downloaded from the internet at the following URL:

http://pubresreg.org/index.php?option=com_docman&task=cat_view&gid=48&Itemid=58

PRRI recommends that in the case of LMOs containing genes stacked by direct transformation or crossing, in which the genes have already assessed previously in individual events, complete safety assessments on the stacked-gene LMO need not start from a blank slate. The information generated in connection with the individual genes can be used to conduct a risk assessment of the combined genes, thus focusing the risk assessment on the potential interactions between genes or gene products. Because the genes and their mode of action are well known, the interactions between introduced genes can be assessed in a precise way. The first step in such an assessment is to determine whether, based on the known characteristics of the gene or gene products, there is a potential for interaction. One example of an identified potential interaction would be the case where the two genes being combined are part of the same metabolic pathway. If the answer is no, then the risk assessment can rely on the previous assessments done on the individual genes. If the answer is yes, then the potential for a harmful or beneficial interaction can be tested. The interactions of these genes with the endogenous genes in the plant can then be assessed in the light of what is known about the interactions of the individual genes and plant genotypes, available from the previous assessments of individual lines. In addition, the assessment can consider information collected from agronomic or other observations that are normally done by breeders. This is a process that has been considered, over many decades of experience, to provide an acceptable level of safety.

This is a reply to 875 RE: stacked genes [#880] - posted on 2008-12-17 11:13 by Beatrix Tappeser

With all due respect I like to contradict the comparison of traditional breeding and genetic engineering. I think this comparison is a categorical fault. Traditional breeding techniques are based on crosses which can occur naturally and combine genes in their existing regulation networks and epigenetic context while genetic engineering has the potential and perceives its attractiveness out of the possibility to introduce new gene cassettes stemming from sources never able to exchange genetic material. (see also definitions in the Cartagena Protocol). There are other laboratory based techniques which have also the potential to combine genomes or part of genomes which can not crossbreed naturally (like cell fusions "beyond taxonomic families, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection" Art.3 Use of terms, Cartagena Protocol) . According to the Protocol these should be assessed with the same scrutiny as a GMO.

According to European law plants with stacked genes have to be assessed on a case by case approach. As Helmut Gaugitsch pointed out in his contribution there are a number of open questions and challenges when assessing plants with stacked genes. Especially the potential interactions – synergistic or antagonistic - between stacked genes and of the stacked genes with their genomic background is methodologically spoken not an easy task to explore. Non GM parent lines, single GM lines and stacked lines have to be compared. In order to assess biological interactions (e.g. effects on non target organism) test designs have to be developed which are based on the use of the whole transgenic plant taking into account the potential receiving environment.

Risk assessors need reliable and comparable data. This needs some form of standardisation of test procedures. There is development work and guidance needed how to choose the right test organisms or develop the right test design, because the current ecotoxicological testing is based on single chemical compounds (pesticide testing). That is a useful starting point but does not suffice to assess complex organism with interacting possibly fortifying or modulating characteristics.

This is a reply to 880 RE: stacked genes [#898] - posted on 2008-12-19 14:42 by Ph.D. Lúcia de Souza

In response to comment 880, it is important to remember that traditionally bred varieties and transgenic varieties do not differ fundamentally in the nature of the risks they may present. This widely recognized and acknowledged fact provides the foundation of risk assessment. First laid out by the OECD1 after many years of expert deliberations, numerous scientific associations worldwide have re-affirmed this principle. It is appropriately embraced in Annex III of the Cartagena Protocol, which states that the risks of LMOs should be "considered in the context of the risks posed by the non-modified recipients or parental organisms". The assumption that traditional breeding combines genes in their pre-existing genetic backgrounds, thus assuring unperturbed gene interactions, is not supported by the facts. There is an enormous body of scientific literature that interspecific and even intraspecific hybrids, an important tool in traditional breeding, often have reduced fitness. This phenomenon is an indication that these genomes, with their co-adapted gene complexes, do not interact perfectly. In fact, the combination and recombination of thousands of genes at a time disrupts regulatory patterns far more than does the introduction of a single gene. This has been confirmed numerous times, with different lines of evidence, most recently by the comparison of metabolic and proteomic profiles between traditionally bred varieties and transgenic varieties (see references 2,3 and 4 for examples). Despite the enormous variety of significant and sometimes drastic genetic manipulation in the course of traditional plant breeding, such breeding has (rightly) been regarded as so safe as to require no regulation in most countries. In fact plant breeders are manipulating thousands of genes routinely without knowing their individual effects or interactions a priori. However, through several cycles of crossing, selection and testing in the field and lab, based on measured traits, productive high quality varieties have been delivered with an acceptable level of safety for centuries. Such an approach can also be applied to transgenic plants.

This discussion of traditional breeding and its impacts serves to provide the baseline for comparison that is the starting point for risk assessment as provided in Annex III of the Cartagena Protocol. The risk assessment that is carried out can then proceed under the framework of Annex III, which can be applied

to both single as well as stacked genes. It is hard to imagine what additional information beyond what is already in Annex III would provide improvements in the risk assessment.

1 See OECD 1986: Recombinant DNA Safety Considerations – Safety considerations for industrial, agricultural and environmental applications of organisms derived by recombinant DNA techniques. ISBN 92-64-12857-3; and OECD, 1993. Safety Evaluation of Foods Derived by Modern Biotechnology: Concepts and Principles. ISBN: 9789264138599. Paris.

2 Lehesranta, S.J. et al., 2005. Comparison of Tuber Proteomes of Potato Varieties, Landraces, and Genetically Modified Lines. Plant Physiology 138: 1690–1699.

3 Catchpole, G.S. et al., 2005. Hierarchical metabolomics demonstrates substantial compositional similarity between genetically modified and conventional potato crops. PNAS 102: 14458 –14462.

4 Batista, R. et al., 2008. Microarray analyses reveal that plant mutagenesis

may induce more transcriptomic changes than transgene insertion. PNAS 105: 3640 –3645.

D. Risk assessment and risk management of LMOs with stacked genes or traits [#874] - posted on 2008-12-14 07:58 by Yasuhiro Yogo

I introduce the concept of risk assessment of LM plants with stacked genes and traits under open field (Type 1 in Domestic Law in Japan).

We consider the effect of LM plants on biodiversity in two generations.

1) The first generation

The traits (genes) of first generation LM plants did not affect on competitiveness, productivity of harmful substances, and crossability, such as herbicide-tolerance, Bt.

As a rule, parental LM plants must be accepted for cultivation under open field.

We judge whether traits of stacked LM plants have any interaction or not.

A) NO

We only judge whether each trait express as well as parental LM plants.

B) YES

We request the ad hoc data based on assumable quantitative and/or qualitative effect of LM plants on biodiversity, and newly evaluate the effect.

In the first generation, multi-stacked LM plants are also evaluated as well as two-way stacked LM plants. In this case, we judge not only multi-stacked LM plants but also intermediate stacked LM plants, including falling out the traits from multi-stacked plants. And when no interaction exists among all assumed combination of traits, we judge the effect on biodiversity as well as A).

The traits, such as male sterile, should be carefully taken into account on falling out from the LM plants, since negative impact to biodiversity will be apprehensive when such traits act alone in plants.

2) The second generation

The traits (genes) of first generation LM plants may affect on competitiveness, productivity of harmful substances, and crossability, such as environmental stress tolerance and quantitative and qualitative growth modification.

In this case, the LM plats is probably judged as it affect on the biodiversity in the Domestic Law in Japan. Therefore we have to carefully evaluate "case by case" more than the first generation. And the restriction of cultivation area and/or monitoring will be imposed.

There are two concepts to judge environmental stress tolerance. We evaluate the effect on biodiversity based on the concept A).

A) Biodiversity under domestic condition: The trials at open field in Japan are needed.

B) Biodiversity under environmental stressed condition: The trials at the condition which reproduce the environmental stress are needed.

Regards

E. Risk assessment and risk management of LMOs with stacked genes or traits [#859] - posted on 2008-12-09 04:41 by Dr KOK GAN CHAN

When there is a stacked gene LMO, risk management involving the detection of all the genes is one concern whether more than one gene should be detected. I opine that the all the genes involved should be detected. However, when there are numerous genes being stacked in a LMO, the may pose a practical consideration to detect a vast number of genes. Also, another concern is on the interaction between/among the genes involved. There is remote possibility when the gene acting along is harmless, but post significant danger when acting in unison.

TOPIC 6 - POST-RELEASE MONITORING AND LONG-TERM EFFECTS OF LMOS RELEASED INTO THE ENVIRONMENT.

Introduction to the topic

by Helmut Gaugitsch, Umweltbundesamt (Federal Environment Agency), Vienna, Austria). E-mail: helmut.gaugitsch@umweltbundesamt.at

Although the issue of potential long-term effects of LMOs released into the environment is regarded as important in the scientific and regulatory debate worldwide, in fact there have been quite few comprehensive studies carried out in this area. Risk assessment frameworks and methods (such as Annex III of the Cartagena Protocol on Biosafety) basically require in an explicit or implicit manner long-term effects to be taken into account but very often do not specify how that should be done. Certain methodological shortcomings are faced when it comes to assessing unanticipated and long-term effects of LMO releases. As a starting point for example there is a wide range of interpretation what long-term in fact means in terms of the time-frame (e.g. years).

A recent study (Cumulative long-term effects of GM crops on human/animal health and the environment: risk assessment methodologies. Central Science Laboratory/UK, 2006) inter alia came to the conclusion that risk assessment focusing on long-term effects must be scientifically valid but also proportionate with respect to cost-effectiveness. Gaps of knowledge primarily cover the need for obtaining solid baseline data as means for comparison. The best indicators have to be identified for that purpose. In addition more in depth-knowledge on introgression into and ecology of wild relatives has to be gained. Improved hazard

identification for long-term and cumulative effects of LMO is another challenge. In most cases the hazards will not be different from those to be taken into account in risk assessment focusing on short-term effects. However, in the long-term also small but complex combination of factors may lead to negative effects and therefore have to be included in a scientific way in hazard identification and risk assessment. Tracking and monitoring cumulative and long-term risks of several LMOs released at the same time and broader stakeholder involvement in the risk assessment process in order to broaden the level of expertise are further challenges to be faced.

A systematic and as far as possible standardized approach based on valid science involving the relevant disciplines is the appropriate way forward and should be pursued nationally and internationally.

For the monitoring of LMOs it is necessary to identify the relevant parameters to be monitored depending on the LMO and its modified characteristics. LMOs, parts of LMOs (e.g. pollen, plant residues) and transgene-products (e.g. Bt-toxins) are able to spread, persist and accumulate in the environment.

As a result specific parameters selected on a case-by-case basis may need to be considered as part of a monitoring plan in order to monitor any establishment into and persistence in non-target environments or ecosystems.

The possibility of long-term persistence and accumulation of LMOs, parts of LMOs and transgene-products in the environment and the potential uncontrolled spread over long distances harbours a major potential for unforeseen environmental impacts, the temporal scale of which currently cannot be estimated. Furthermore, they are important indicators for cumulative effects.

Recording and monitoring dispersal, persistence and accumulation of LMOs, parts of LMOs and transgene-products in the environment may not primarily provide documentary proof of an adverse impact of an LMO but may be necessary in a precautionary documentation of a process, which may entail adverse environmental effects in the future. It provides knowledge on dispersal pathways of LMOs, parts of LMOs and transgene-products into media in which they possibly can survive, reproduce, multiply or accumulate.

For certain LMOs with specific traits (e.g. LMOs producing pharmaceutical substances, e.g. pharma crops), the tracing of not only the LMO itself or its transgene products but also of transgenic sequences in the environment might be also relevant as also the sequences may entail potential adverse effects on the environment, human or animal health.

Thus the information gained from monitoring of LMOs, parts of LMOs or transgene products represents an important basis for drawing conclusions on interrelationships between unforeseeable environmental effects either occurring immediately or those occurring with a time-lag and the environmental release of a LMO. Thus the detection and monitoring of LMOs, parts of LMOs and transgene-products in different environmental compartments are an essential element of LMO monitoring.

Like for the risk assessment, monitoring should be performed by systematic and standardized procedures, based on scientific experience and knowledge.

Suggested points for discussion

- Time and spatial (e.g., how often and for how long) requirements for monitoring different types of LMOs, traits and receiving environments;
- How to assess long-term effects of LMOs?
- What type of baseline data is needed and how to develop it?

- Other considerations regarding post-release monitoring and long-term effects, including emergency measures, that should be taken into account when preparing risk assessment reports.

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Interventions

A. Welcome to the second round of discussions [#845] - posted on 2008-12-01 00:57 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Post-release monitoring and long-term effects of LMOs released into the environment".

The discussions within this group will take place from 1 to 14 December 2008.

To assist in the discussions, the following is a non-exhaustive list of suggested points for discussion:

1. Time and spatial (e.g., how often and for how long) requirements for monitoring different types of LMOs, traits and receiving environments;

2. How to assess long-term effects of LMOs?

3. What type of baseline data is needed and how to develop it?

4. Other considerations regarding post-release monitoring and long-term effects, including emergency measures, that should be taken into account when preparing risk assessment reports.

Also, an introduction to the topic, as well as a non-exhaustive list of suggested reading materials have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum is available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

The CBD Secretariat thanks you for your active participation. Happy discussions!

The Biosafety Division

B. Post-release monitoring and long-term effects of LMOs released into the environment [#881] - posted on 2008-12-17 12:51 by Hajara - Yusuf Sadiq

Dear Colleagues,

In respect to the ongoing discussion on post-release monitoring and long-term effects of LMOs released into the environment.

My opinion is that, it all depends on the kind of LMOs to be released into the environment which will determine how to monitor its release and its long-term effects.

In the process of doing post-release of LMOs monitoring, one question always come to mind as 'Is LMOs present in the material of interest, and how much of it is present? This is the first step in assessing whether the presence of a given LMOs is correlated with specific effects either on the environment or on health. The ability to monitor LMOs in the environment is therefore an essential capacity required for biosafety assessment.

Hajara Yusuf Sadiq

National Biotechnology Development Agency

Abuja-Nigeria

This is a reply to 881 RE: post-release monitoring and long-term effects of LMOs released into the environment [#882] - posted on 2008-12-18 18:27 by Prof. Dr. Kazuo Watanabe

There could be two categories for discussion

1) LMOs-FFP which have been released a long time ago with a decade of commercial experience
2) LMOs under experimental trial under the confined environment or semi-closed condition such as isolated field or pond.

As for 1) There is more than ten years of experiences in many crop producing countries. Compilation of information as review shall be at first with the elements/modality listed in Annex III of RA. With that there may be elements to be enforced to examine the long term effects. There shall be a distinction of LMOs presence and the released environment and methods such as cultivation/agriculture system as that there was some confusion of the interpretation of the assessments in the past.

2) This may be yet within of the context of RA rather than monitoring, since there are many experience of trials, there could be some compilation of modalities to summarize the common features and specific features.

regards,

K. Watanabe, Japan

This is a reply to 882 RE: post-release monitoring and long-term effects of LMOs released into the environment [#890] - posted on 2008-12-19 08:16 by Hiroshi Yoshikura

1. The interaction of LMOs with other organisms and environment is complex, and just monitoring the survival of LMOs in the environment is often meaningless. Therefore, when monitoring is considered,

"its need and utility should be considered, on a case-by-case basis, during risk assessment and its practicability should be considered during the risk management. The monitoring may be undertaken for the purpose of:

a) verifying conclusions about the absence or possible occurrence, impact and significance of potential environmental effects; and
b) monitoring changes in environmental parameters (that are deduced from the conclusions of the risk assessment) to determine their environmental impact."

The sentence in the quotation marks is modified (underlined part) from paragraph 20 of Principles for the Risk Analysis of Foods Derived from Modern Biotechnology.

2. The objectives of monitoring and parameters to be monitored should be first identified through the process of risk assessment. "Time and spatial (e.g., how often and for how long) requirements for monitoring different types of LMOs, traits and receiving environments" should meet the objectives and should be practicable.

The type of baseline data is needed is the natural history of non-modified recipients or parental organisms.

This is a reply to 881 RE: post-release monitoring and long-term effects of LMOs released into the environment (what and how ?) [#894] - posted on 2008-12-19 10:01 by Beatrix Tappeser

In respect to the ongoing discussion on long-term effects of LMOs released into the environment my opinion is that it depends on the species, the potential lifetime (annual or long-living crops and trees), modified traits (herbicide-tolerance, inclusion of an insecticide, altered substances of content) and the intended use of the LMO (import only, processing only or cultivation). So this should be assessed by the authorities on a case-by-case basis.

Protection targets:

Monitoring should be primarily directed towards environmental protection targets, for instance conservation of the biological diversity in terrestrial and aquatic ecosystems, conservation of especially endangered or protected species, habitats or ecosystems, conservation of soil functions and soil biocenosis or human health. Terrestrial agro-ecosystems, aquatic ecosystems and air are strongly merged on the one hand and on the other hand they are also closely linked with other items such as human health, cultural and real assets, utilisation of the environment or the natural landscape. Conservation of biodiversity and respective ecosystem functions, I think, are among the most essential protection targets.

Selection of indicator organisms:

The essential step is to identify appropriate indicator organisms for long-term LMO effects. An important criterion for their selection is the potential to indicate LMO-induced changes. This potential may depend on

a) direct and/or indirect interrelationships with the LMO
b) a preferably widespread distribution of the indicator,
c) sufficiently high abundance
d) importance for ecological processes and ecosystem functions.

Another important aspect is the feasibility, economy and standardisation of detection methods.

To make selection criteria transparent they can be systematically assessed within a matrix (there are examples how this can be done)

This is a reply to 890 RE: post-release monitoring and long-term effects of LMOs released into the environment [#901] - posted on 2008-12-19 15:31 by Ricarda Steinbrecher

Dear colleagues,

I agree with Hiroshi Yoshikura that "the objectives of monitoring and parameters to be monitored should be first identified through the process of risk assessment."

With this I mean, that the need for and the ability of performing post release monitoring of both the spread of the LMO, its genes and/or traits as well as of its impacts on the environment, biodiversity or human health needs to be integral part of the risk assessment procedure.

The need for the ability to (1) monitor gene escape and the ability to (2) understand, anticipate and guard against long-term negative effects is evident for example in the case of genetically engineered trees.

(1) In order to be able to monitor gene escape, the extent, routes and means of gene flow must be understood. Whilst more, [though maybe not sufficient,] is known for some annual agricultural annual crop plants, the understanding of gene flow from trees is still very limited and does not allow predictions. The question thus arises of how to perform post release monitoring in cases where both time and special requirements are enormous and little detail of when and where to look is available.

In the case of trees it is evident, that propagative plant material will travel and cross national borders. Thus risk assessment and post release monitoring, risk decisions and risk management need to be carried out in a "beyond national boundaries" process, also in the understanding that long-term effects will not be limited to the release site but potentially manifest across borders.

To recall (see also Steinbrecher & Lorch 2008),

most trees and their genes will spread not only through sexual reproduction (pollen and seed) but also by asexual (vegetative) reproduction, such as roots, shoots, twigs that can set root. These propagules can be dispersed by wind, water, pollinators (insects), animals and humans. To assess possible contamination a wide range of factors need to be taken into account, ranging from normal weather conditions in which pollen and seeds already travel long distances (depending on direction, speed and uplift of the wind), to extreme conditions like storms and floodings in which broken branches are swept along and can set root somewhere else. Animals and humans also attribute to the spread of seeds when they either take fruits, nuts, cones along (such as squirrels), or even when they consume fruits, thereby passing the seeds through their body and depositing them somewhere else.

"In any event, as we deploy vast plantations of transgene-bearing forest trees, we can expect the transgenes to escape into the wild population and to persist there for a long time. In conclusion, we can probably take the view that 'propagules will travel'." (Smouse et al. 2007)

The issue is not only contamination, but also invasiveness, especially where pioneer species such as GE poplar or birch are modified such that they gain an advantage over wild trees of the same or of other species. An example of a transgenic trait that can confer an advantage is cold tolerance (developed in eucalyptus), allowing trees to be cultivated in colder regions and thereby potentially enabling them to get established in ecosystems where this tree species previously did not grow or maybe where trees in general did not grow. Other examples are trees producing insecticidal protein (e.g. Bt toxins) and therefore possibly (more) resistant to specific pest insects, and trees with faster growth or bigger leaves who can out-compete other tree seedlings competing for light and space in forest settings.

"Transgenes which provide a large fitness advantage, perhaps by protecting from herbivores or disease, may enhance invasiveness." "Transgenes which enhance fitness are most likely to increase invasiveness and frequency of recipient species outside cropping system." (James 1998, see also Andow & Zwahlen 2006).

Pollen

Forest trees are largely wind-pollinated, with pollen highly adapted to be transported by wind, often over large distances. Whilst for white spruce (*Picea glauca*), the vast majority of pollen was found to cross-pollinate within a range of 250-3000m (O'Connell et al. 2007), travel distances of 1000 km have been documented for spruce pollen (Gregory 1973) and 100s of kilometres for birch pollen. For risk assessment purposes, pollen dispersal rates cannot be taken into account for individual years only, but have to be looked at cumulatively over time, e.g. a long distance dispersal (LDD) rate of 1% would amount to 9.6% over the period of a decade (Smouse et al. 2007).

Seed dispersal

Seed dispersal needs to be taken into consideration when looking at gene flow. For trees we find, that they have developed a multitude of strategies to have their seeds dispersed either by abiotic means, such as wind or water, or by biotic means, mostly animals including humans.

Trees, especially forest trees, produce large quantities of seeds often well adapted to wind dispersal (abiotic seed dispersal). For examples as well as for vegetative propagules dispersal see attached paper Steinbrecher & Lorch (2008).

(2) In order to understand, anticipate and guard against long-term negative effects, it appears crucial to avoid assumption based prognosis. For this purpose it is crucial to have detailed and long term experience with the conventional parental plant of the LMO in question, thus any behavioural changes can be detected instantly and acted upon if necessary. Furthermore detailed and long-term experience is also required for the environmental and biodiversity settings and interactions in which the plant is commercially grown and/or naturally occurs. Whilst this strikes as common sense and might appear an easy task in particular cases, it is far from easy – if not currently impossible - in other cases, such as transgenic trees in the context of global forest biodiversity and global forest ecosystems.

In this context it is also important to remember, that a trait-confined risk assessment is insufficient for transgenic trees, where The ability to respond to biotic and abiotic stresses may be compromised by the performance of the transgene, its product(s) and the processes of genetic engineering. Vice versa, such stresses may also interfere with the performance of the transgene, e.g. induce gene silencing (Broer 1996, Meza 2001)

Testing for any impacts on tree performance (internally as well as externally) will (or would) require a long time and additionally necessitate exposure to all different stresses across different developmental stages.

To summarise, the ability to carry out reliable post release monitoring, including assessing gene flow, and the ability to investigate and safeguard against long-term negative effects need to be assessed in the initial risk assessment itself. If data are insufficient or results are unsatisfactory, further research is required, especially to have all necessary base line data. However, to complicate matters further, field research must only be undertaken in a way that does not pose a risk to the environment in itself.

Literature cited:

Andow DA & Zwahlen C (2006). Assessing environmental risk of transgenic plants. Ecology Letter 9(2): 196-214.

Broer I (1996). Stress inactivation of foreign genes in transgenic plants. Field Crops Research 45: 19-25

Gregory PH (1973). The microbiology of the Atmosphere. 2nd edition. Leonard Hill, Aylesbury, UK. (In OECD consensus document vol 2, p.208).

James R, DiFazio SP, Brunner AM & Strauss SH (1998). Environmental effects of genetically engineered woody biomass crops. Biomass and Bioenergy 4(4): 403-414.

Meza TJ, Kamfjord D, Hakelien AM, Evans I, Godager LH, Mandal A, Jakobsen KS, and Aalen RB (2001). The frequency of silencing in Arabidopsis thaliana varies highly between progeny of siblings and can be influenced by environmental factors. Transgenic Research 10: 53-67

O'Connell LM, Mosseler A, and Rajora OP (2007). Extensive Long-Distance Pollen Dispersal in a Fragmented Landscape Maintains Genetic Diversity in White Spruce. Journal of Heredity 98(7): 640-645 (doi:10.1093/jhered/esm089)

OECD (2006). Safety assessment of transgenic organisms: Consensus documents on the biology of trees. OECD Consensus Documents Volume 2 (1996-2006), Chapter 4.

Smouse PE, Robledo-Arnuncio JJ & Gonzáles-Martines SC (2007). Implications of natural propagule flow for containment of genetically modified forest trees. Tree Genetics & Genomics 3(2): 141-152.

Literature attached:

Steinbrecher & Lorch: Genetically Engineered Trees and Risk Assessment – An overview of risk assessment and risk management issues. Federation of German Scientists, May 2008. Available at http://www.econexus.info/pdf/GE-Tree_FGS_2008.pdf or http://www.ifrik.org/en/gm-trees-risk-assessment

This is a reply to 901 RE: post-release monitoring and long-term effects of LMOs released into the environment [#904] - posted on 2008-12-19 15:53 by Dr Thomas Nickson

I am Tom Nickson, a scientist who has worked with Monsanto Company for over 27 years and an environmental risk assessment expert for biotech crops with over 16 years experience. I have studied the overview and contributions to this subject of post-release monitoring and long-term effects with great interest. It appears to me that a critical concept has not yet been mentioned, which is the role risk assessment plays in directing the monitoring and necessary post-release activities. As such, this is not so much a specific reply as it is a comment on the entire topic.

Some important ideas have been put forward in the overview statement. Firstly, a recent study "came to the conclusion that risk assessment focusing on long-term effects must be scientifically valid but also proportionate with respect to cost-effectiveness." Implicit in this statement is that knowledge has limits and science, even when it is "valid", leads to additional questions. Efforts to answer these questions, as

well as the answers themselves will have associated costs. These costs can be described in terms of regulatory and other resources, as well as lost opportunity to growers and the environment that could benefit from improved practices. This cost-benefit must be balanced within a country where both the impacts of the costs and benefits are realized. As such, post-release monitoring has broad cost implications that must be considered, and these should be guided by risk assessment.

A second important point made implicitly in the overview is that in any decision-making there will be some degree of uncertainty or unknown possibilities at the time a decision is made. It states, "[t]he possibility of long-term persistence and accumulation of LMOs, parts of LMOs and transgene-products in the environment and the potential uncontrolled spread over long distances harbours a major potential for unforeseen environmental impacts, the temporal scale of which currently cannot be estimated." This statement reflects a one-dimensional view of the uncertainty. In fact, there would likely be just as much uncertainty around the long-term environmental impact associated with a "no" decision or delayed decision.

At a high level, it is logical that some may see monitoring as a means of dealing with this uncertainty. However, this should only be done with careful consideration and reflection on some basic assumptions. When considering making a request for monitoring, a regulatory authority must ask first ask the questions of what needs to be monitored, how it should be monitored, how long it should be monitored, where it should be monitored and what would an adverse outcome of the monitoring look like? Importantly, each of these questions should be informed by a risk assessment, which itself would be guided by policy covering environmental protection. These critical questions on monitoring may be more appropriately dealt with as questions about potential unforeseen and even unpredictable environmental impacts that are better addressed through basic research. Failing to guide the risk assessment/risk management process using a policy-driven structure results in confusion, excessive costs and can even result in regulatory action based on wrong information. Requirements on post-release monitoring should be an outcome of a process where risk assessment informs the various components of the decision, resulting in any necessary and appropriate actions.

In summary, we must take care to not confuse the regulatory requirement of monitoring with an exercise in conducting basic environmental research. Regulators must avoid the temptation to pursue what might be nice to know with what they need to know in order to make a defensible and cost effective decision regarding regulatory approval, and use the risk assessment to guide them in decisions on monitoring. In the context of the risk assessment and risk management under the Protocol, monitoring should be seen as a regulatory activity guided by the risk assessment that is guided by policy-based environmental protection goals, and science is the tool to collect information.

This is a reply to 901 RE: post-release monitoring and long-term effects of LMOs released into the environment [#906] - posted on 2008-12-19 16:00 by Dr. Les Pearson

I realize that the deadline for postings is very short so this is a brief message.

With respect to GM trees it seems that the impression given is that ALL trees have long pollen or seed dispersal, can be propagated from vegetative materials and other attributes. This is simply not the case. Each species must be considered based on its specific characteristics on a case-by-case basis.

C. Monitoring and long-term effects [#900] - posted on 2008-12-19 14:44 by Dr Marja Ruohonen-Lehto

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Dear colleagues,

My name is Marja Ruohonen-Lehto and I work as a Senior Adviser in the Finnish Environment Institute. I have almost 15 years of experience in environmental risk assessment of LMOs/GMOs. I have also been actively participating in the EU (Commission) working group on monitoring and been responsible together with colleagues from Austria, Belgium and Italy in developing specific monitoring guidance for oilseed rape (*Brassica napus/rapa*).

I am sorry that I only now, at the last moment, have the possibility to join (due to other obligations and travelling) the discussions. However, I think that the discussions have been excellent and I do not necessarily have a lot to add. The main issues of monitoring have been taken up: good planning, representative regions, scientific approach to data collection (statistical power of replicas and sample sets), baseline information and data, standardized methods, possibility to use available/already existing e.g. environmental monitoring programs, choosing indicator species for different geographical regions, feasible time used for monitoring and last, but not least, practical monitoring plans that can be carried out properly. This is of course not an exhaustive list.

The most important thing in monitoring is that your monitoring plan/regime can really give an answer to the questions that you are asking. A lot of emphasis should be given to planning of scientifically sound monitoring regimes. It is often stated or argued that monitoring is not scientific research and this is true of course. However, we do have a perception of possible adverse effects and uncertainties linked to LMOs/GMOs and these are the very issues that should be monitored. And they must be monitored with scientifically sound methods and approaches.

D. Post-release monitoring and long-term effects of LMOs released into the environment-Issues to be considered [#873] - posted on 2008-12-13 05:52 by Dr Kok Gan Chan

Dear colleagues,

With regards to the time period to monitor the LMO released to the environment, presumably deliberate release ones, there is no hard and fast rule as to the time frame for monitoring.

By and large, it depends on the LMO itself, with specific reference to its life span in the wild, also its other propagative forms such as seed and spores etc which can endure years in the environment. These must be monitored as well. And surely it will involve monitor programs that last for years.

Not to forget the cost involved to monitor the LMO and its other propagative forms. Too frequent the monitoring increases the cost, otherwise it may amount to non-monitoring and allowing risk to go unchecked.

I suggest a general surveillance monitoring can be done frequently, in combination with a less frequent, case-specific monitoring.

The data obtained from each monitoring should be combined, in which the minister-in-charge or national centre on biosafety should compile these data for further and related monitoring. Sharing of these data at international level on a common platform, says on a particular webpage(s) will facilitate trans-national data sharing.

Sure enough, we are only looking at one perspective i.e. time-period of monitoring, there are more to be done.

Regards,

Dr Kok-Gan Chan,

Senior Lecturer, ISB (Genetics & Molecular Biology)

Faculty of Science, University of Malaya

This is a reply to 873 RE: Post-release monitoring and long-term effects of LMOs released into the environment-Issues to be considered [#899] - posted on 2008-12-19 14:44 by Ph.D. Lúcia de Souza

Monitoring should not be assumed to be necessary in all cases, but should be imposed if there is a clear need for such activity, based on a thorough risk assessment. In the case of LMOs that have been determined to be safe enough to deploy into the environment (keeping in mind that the non-modified organism is the baseline comparator), there should be no need for monitoring. In those cases where monitoring is necessary, there should be a clear formulation of the environmental variables that should be monitored, the endpoints to be measured, and their relationship to the protection goals of a country.

E. Gene Flow [#897] - posted on 2008-12-19 13:08 by Ph.D. Lúcia de Souza

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Reflecting on the ecological consequences of the gene flow: one should consider the potential exposure and hazard. The likelihood of gene flow occurring is often considered as the probability of exposure in the risk assessment equation. Gene flow can occur, through the pollen or through admixtures of seed, or volunteer plants. For gene flow to occur each of the following events must take place:

1. Pollen (male) must effectively be transferred onto a sexually compatible pistil (female);
2. Fertilization must occur and a viable seed must develop;
3. The viable seed must dehisce and in an acceptable environment for germination;
4. The seed must germinate and establish a fertile plant;
5. The fertile plant must be pollinated and in turn produce a viable seed;
6. The viable seed must germinate and produce a plant.

If any of these events fails, pollen-mediated gene flow will not happen, and seed-mediated gene flow will not occur if events 3 to 6 are not met. The likelihood of gene flow is affected by sexual compatibility, the distance of sexually compatible plant species, pollen viability/longevity, coincidence of flowering, presence of pollen vectors (wind or insect), relative size of populations and gene frequencies within the populations.

Research trials have a very low risk as exposure is dramatically reduced compared to commercial releases, mainly because of their small size and the imposed isolation measures. In the context of regulated environmental release, field trials make up a very small portion of total land area. Furthermore confined field trials are conducted in such a manner to reduce risk of escape. By this argument even the so called “high” risk outcrossing plant has near zero risk regardless of trait.

A transgene can under a combination of certain conditions: - be transferred; and be expressed; and persist and disseminate to a related wild relative through further hybridization and introgression. This is not different from the case of traditional domestication-traits that were either unconsciously or intentionally selected and changed by man during thousands of years. When domestication traits including loss of seed dispersal, synchronized pod shattering, loss of seed dormancy, failure of protection against herbivores (lowering of toxic substances such as in cassava, potato…), herbicide resistance, rapid growth, early flowering, increased grain yield, etc. are spread to wild relatives, ecological consequences are possible. It is important to keep in mind that certain traits developed through modern biotechnology have also been produced through traditional breeding (e.g. resistance to herbicides, herbivores, pathogens and adaptation to new environments). It is useful to compare the knowledge gained on the effects of conventionally bred, i.e. non-transgenic crop genes that passed to the wild to the effects of LMOs. Decades of breeding in multiple crops has shown little effect from gene flow. Even for traits that one

would suspect would have a selective advantage such as disease resistance, wild species have not uniformly become disease resistance. This could be because consistent disease pressure, i.e. a consistent natural selective advantage, is not present. This is the kind of information to consider when assessing the risk from gene flow, whether from GM or conventional breeding.

The possibility of introgression of a transgene might increase when there is a certain combination of conditions (such as significant possibility of hybridization between GM and wild relative and a resulting fertile and fit progeny). It is part of the risk assessment (as described in Annex III of the CPB) to consider the likelihood of a transgene to spread and to persist and to consider the potential environmental consequences (the hazard) associated with gene flow from an LMO to compatible plants. This is the reason to consider several points such as biological characteristics of the recipient organism, the introduced trait, characteristics of the receiving environment such as centres of origin and genetic diversity, description of the habitat where organisms may persist or proliferate, etc. If the resulting plant is likely to cause a negative impact to the specific ecosystem, measures or activities to manage the potential risk should be considered. It is in the case of related weedy species in agro-ecosystems: con-specific weeds, or at least sharing one genome of amphiploid (for example with rice/weedy rice, sorghum/shattercane and Johnsongrass, sunflower/weedy sunflower, wheat/Aegilops cylindrica, beets/wild beets) when sexually compatible that the risk of gene flow is higher. It is in these cases that efficient containment and mitigation strategies should be considered, as the weedy species are typically adapted to maximize gene flow, especially when there is a selective advantage. The consequences of gene flow is trait dependent. Traits that do not alter the fitness of the plant in any way may not be likely to have an impact even if the recipient plant is a weed.

Documents describing the biology of crops (for example the OECD consensus documents) are important to decide on the introduction to a specific environment and on the risk management options. There are already some on major crops (such as maize, soybean, rice,….) and the development of such documents on other, including major agricultural crops (such as sugar cane, Phaseolus, cowpea, Cassava, ….), as well as minor crops or specialty crops that will be the subject of a regulatory decision, is very important.

Concerns on the effects of gene flow in specific cases is not limited to genetically engineered crops, but in the case of transgenic plants, new technologies including molecular tools (e.g. GURTs, targeted transformation, etc.) are under development. The potential risks associated with gene flow could be reduced even further.

F. Harmonising monitoring approaches and data" and "Developing baseline data [#893] - posted on 2008-12-19 09:58 by Beatrix Tappeser

Dear Colleagues,

I argue that a harmonised monitoring methodology should be focussed and agreed upon as to produce comparable information across different nations.

Once LMOs are monitored, different types of data will accumulate, which need to be centrally collected and efficiently processed. The data need to be compared to each other including baseline data and statistically analysed to assess potential adverse effects. This requires a minimum common standard for data quality, for instance on data pre-processing stage, number of replications and statistical power. And the data should if possible be based on standardised methods to be comparable. Comparability and good quality of data require a broad-scale international harmonisation approach, for instance using existing ISO standards of methods, data storage and structuring.

The inclusion und use of existing agronomic and environmental monitoring programmes to monitor LMOs is worth thinking about, too. Some of them use standards. They can provide useful baseline data over many years and different sites.

Secondly,

In respect to the question of how baseline data may be developed I am sure that we all agree that determining the baseline status of a LMO field and its environment exposed is a prerequisite for identifying adverse changes.

1. This baseline status may be registered prior to LMO release and then long-term monitoring of the LMO areas may exhibit adverse changes.

2. An alternative is the split field design and comparable long-term LMO-free reference areas which has been done for instance in the UK Farm Scale Evaluations. I consider parallel observations a must in order to reduce the background noise data induced by the high dynamic in agricultural practice and landscapes.

Both long-term time series monitoring after baseline analysis and parallel monitoring of LMO areas and LMO-free areas can ideally complement one another.

G. Where to monitor: spatial requirements [#892] - posted on 2008-12-19 09:53 by Beatrix Tappeser

Dear Colleagues,

In respect to the ongoing discussion my opinion on the spatial aspects of LMO monitoring is that it should take place in exposed areas, preferably cultivated fields plus their environment. The number of monitoring sites and regions needs to be sufficient to support statistical analysis of results based on good scientific practice. For every LMO the monitoring design and data analyses could (and maybe should) be based on a specific scale, quality and quantity of data to be representative and interpretable. This requires flexibility with the monitoring design. Monitoring every LMO everywhere is neither necessary nor feasible. If the sites and regions are adequately distributed an intelligent systematic monitoring design can be repre-sentative for large areas. Criteria for selecting monitoring sites and regions may include

a) representativeness of sites intensively cultivated with LMOs,
b) representativeness of ecological regions containing the spectrum of selected potentially adversely affected indicators,
c) availability of sites already monitored within cultivated other agro-environmental programmes
d) areas with favourable environmental conditions facilitating spread or survival of GMOs

This requires availability of thematic geographic data containing this information like ecoregion maps, land cover data, agricultural census data and the good knowledge of the LMO-cultivated fields.

The spatial selection of monitoring sites can also include the aspect cumulative and/or long-term effects (sites which remain repeatedly cultivated over years).

H. Assessment and long-term monitoring of recombinant vaccines [#886] - posted on 2008-12-18 22:28 by Shigeki Inumaru

I have been working at National Institute of Animal Health, Japan, so I am concerning about recombinant vaccines for veterinary use.

It is indispensable to assess leakage of recombinant microorganisms and viruses, and to perform long-term monitoring. Accuracy of the assessment and monitoring restrict the allowable vaccines. We have no experience about these issues, since no commercial recombinant vaccine for veterinary use is purchased in Japan now. So, I like to ask about the experiences and knowledge about the systems, methods and so on, related to the matter.

Shigeki Inumaru, Japan

I. Cuba´s opinion in relation to the topic Post-release monitoring and long-term effects of LMOs released into the environment [#870] - posted on 2008-12-12 15:45 by Leticia Pastor Chirino

Dear colleagues

Please, I would like to express Cuba´s opinion in relation to the topic Post-release monitoring and long-term effects of LMOs released into the environment.

Tacking into account the negative consequences that LMOs could have for the environment and human health, and bearing in mind also, the fact that the monitoring procedures play an important role in the prevention of these effects, the surveillance and monitoring of these adverse effects are mandatory in the case of Cuba. This is stated in the national legislation on Biosafety.

Currently, We are working hard on the implementation of a monitoring system in Cuba. Although it is in a primary stage so far, this system is aimed at organizing, guiding and homogenizing the behaviour to be followed by the applicants for the biosafety authorizations, the specialist from the regulatory body and other stakeholders, regarding monitoring of the possible adverse effects of LMOs. This system will make easier the collection of data and the evaluation of the mechanisms applied to the specifics cases, in order to design more specifics monitoring systems based on previous experiences.

The surveillance and monitoring must be designed so as to allow the detection of the variability in the populations subjected to the monitoring, from incipient stages. These populations will depend on the LMO in question, the recipient environment and the identified adverse effects. No matter how long the appearance of these effects take, the monitoring systems must be able to detect them at the earliest possible moment, in order to undertake the appropriate mitigation and elimination activities.

Sometimes these adverse effects result in irreversible damages become apparent in the long term. When this is the case, the management of these consequences can be very expensive and to hard to handle. that is the reason why the monitoring system is the responsible for the timely detection of the adverse effects. Sometimes and for some cases, these monitoring systems can be the same ones that are used permanently. These ones will detect only a little different aspects in the population subjected to the monitoring, which will conduct to the need of more specifics tests to be undertaken in order to establish the cause-effect relationship with the LMO.

In the case of Cuba, for the adverse effect on human health, the current monitoring systems applied to the public health in a general sense, could be enough for dealing with LMOs which potentially affect the human health.

Best regards

Drab. Leticia Pastor Chirino.

National Centre for Biosafety. Cuba.

J. Gene flow [#858] - posted on 2008-12-09 02:00 by 魏 伟

What I much concern is gene flow and its ecological consequence. Long-term effect is much hard to work on. Most confident and hard works and assessments should be finished before large release. Gene flow could spontaneously happen in nature but could be in low probability. However, small probability event could result in high damages. To simulate this process in a short period we can manage to obtain advanced generation of the hybrids and backcross between crop and wild relatives. The fitness of these plants will be assessed in the simulation of field situation with competition under certain circumstances.

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TOPIC 7 - RISK ASSESSMENT AND RISK MANAGEMENT OF SPECIFIC RECEIVING ENVIRONMENTS

Introduction to the topic

by Dr. Amanda Gálvez Mariscal, Universidad Nacional Autónoma de México, Mexico. Email: galvez@servidor.unam.mx

The receiving environment plays a major role in the determination of potential risks in the deployment of GMOs. It is also an important factor in the development strategies to minimize the effect of potential risks. Biosafety research takes into consideration parameters such as crop to crop gene flow, crop to weed gene flow, crop to wild relative gene flow as well as indirect effects on wildlife biodiversity, soil and water in the process of assessing the potential risks.

There is need for research into the fate of transgenes over time in recipient wild relatives or native varieties. Also great attention should be given to specific areas where in situ germplasm collections are kept to prevent possible introgression of transgenes into these collections.

Virtual collections of information on the biology of wild and domesticated plants have been developed and provide useful baseline information for assessing the safety of GMOs in specific receiving environments.

Also of specific interest in risk assessment and risk management processes are the centres of origin and diversification. Biodiversity in centres of origin is a crucial factor to consider in risk assessment and management, especially when dealing with territories where domesticated varieties are found, and in which wild relatives and native species of economical importance still co-exist.

Three major areas of domestication and diversification are identified [references 1,2]:

a. The so called Fertile Crescent in the Nile Valley of Egypt, eastward across Syria and Iran to the Persian Gulf where wheat (Triticum), barley (Hordeum), pea (Pisum), lentil (Lens) and vetch (Vicia).
b. South East Asia: Thailand and China, in the Yangtze River area for rice (Oryza), soybean (Glycine), millet (Pennisetum), sugarcane (Saccharum), rape (Brassica), hemp (Cannabis).
c. And in the American continent, in Mexico and Peru: corn (Zea), squash (Cucurbita), tomato (Lycopersicon), beans (Phaseolus), white potato (Solanum), sweet potato (Ipomoea), chili peppers (Capsicum), peanut (Arachis), guava (Psidium), avocado (Persea), cotton (Gossypium).

A special consideration must be given to parameters such as baseline of wild relatives of the GM crop in centres of origin, baseline of native/domesticated varieties of the crop while undertaking risk assessments at the centres of origin. The determination of the rate of gene flow in a complex system of wild and domesticated plants is challenging [reference 3] as well as the sampling procedures.

Cited references

1. http://arnica.csustan.edu/boty3050/Notes/origins.htm
2. CONABIO. 2008. Listado de especies de flora para las cuales se ha documentado que México es centro de origen, de diversidad genética o de domesticación. Coordinación de Análisis de Riesgo y Bioseguridad. 12 p.
3. Ellstrand, N.C. et al. (1999) Gene flow and introgression from domesticated plants into their wild relatives. Annu. Rev. Ecol. Syst. 30: 539-563.

Suggested points for discussion

- Special considerations that should be taken into account when assessing the safety of LMOs to be introduced into specific environments, such as centres of origin or diversity, fragile ecosystems, small islands, etc.
- How to develop baseline data?
- Other considerations regarding such specific receiving environments, including emergency measures, that should be taken into account when preparing risk assessment reports.

List of threads and number of replies

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G. Developing an approach of defining "receiving environments" 0

Interventions

A. Welcome to the second round of discussions [#842] - posted on 2008-11-30 22:37 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Risk assessment and risk management of specific receiving environments".

The discussions within this group will take place from 1 to 14 December 2008.

To assist in the discussions, the following is a non-exhaustive list of suggested points for discussion:

1. Special considerations that should be taken into account when assessing the safety of LMOs to be introduced into specific environments, such as centres of origin or diversity, fragile ecosystems, small islands, etc.

2. How to develop baseline data?

3. Other considerations regarding such specific receiving environments, including emergency measures, that should be taken into account when preparing risk assessment reports.

Also, an introduction to the topic, as well as a non-exhaustive list of suggested reading materials have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum is available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

The CBD Secretariat thanks you for your active participation. Happy discussions!

The Biosafety Division

B. Risk assessment and risk management of specific receiving environments – with particular relevance to transgenic trees and forests [#889] - posted on 2008-12-19 08:14 by Ricarda Steinbrecher

My name is Ricarda Steinbrecher, representing the Federation of German Scientists. I have participated in the negotiations and deliberations surrounding the Cartagena Biosafety Protocol since 1995, with a particular focus on risk identification and risk assessment.

In the context of the discussion on specific receiving environments I want to raise some particular aspects concerning the case of LMOs being genetically engineered (GE) trees.

Some might argue that for annual crops the consideration of different specific receiving environments would be interesting, but that one could do without, but for GM trees it is key that receiving environments play an important role in their short and long term risk assessment.

In the case of GE trees a distinction may have to be made between intended and unintended receiving environment.

It has been well documented, that trees differ significantly from annual agricultural crops, in particular (see also Steinbrecher & Lorch 2008, attached):

1) Trees have a low level of domestication (El-Kassaby 2003 in Sedjo 2006, Libby 1973 in FAO 2004). Unlike (domesticated) field crops, trees can persist and establish in the wild, in unmanaged ecosystems (Finstad et al. 2007);
2) Trees have a life cycle of decades or centuries; with life spans ranging from 150-300 years (Balsam Poplar, Silver Birch, Loblolly Pine, American Elm) to 3000-3500 years (Giant Sequoia, Alaska Yellow Cedar). Even managed trees in plantations have a life span of up to several decades. Depending on tree species, seed production may start as early as at age 4 or as late as 30. Pollen and seed production increase greatly with age and height.
3) Pollen, seed and other reproductive plant materials are dispersed over long distances, e.g. dispersal of seed from conifers has been reported over distances as far as 600 to 1200 km (Katul et al. 2006). (see also my contribution in discussion group on PRM/LTE).
4) Trees have a large spatial distribution: many trees are present over a large geographical area and hybridisation is common. This is especially true for the genus *Populus*.
5) Trees are integral part of complex ecosystems – forests: Field crops are part to mostly tightly controlled cropping systems, with reduced or minimized interaction with other organism (plant, animal, fungi or bacteria). Trees, however, are a major part of complex and diverse ecosystems (forests), also providing ecosystems, habitats and food to symbiotic partners, such as mycorrhiza, and for animals and other plants. Unlike most agricultural plants, forest trees can persist and thrive in unmanaged ecosystems.
6) Trees affect water and climate systems: forests play essential roles in managing water supply and rainfall, carbon sequestration and also climate regulation.

Due to these characteristics, the receiving environments play an important role. A risk assessment of GE trees for a particular environment or geographical location cannot be regarded as sufficient, but needs to be extended to potential impacts on the emergence of the transgenic trees or their transgenes and otherwise altered DNA, in natural or managed forests and woodlands. Forests and woodlands, both managed and unmanaged, should thus be categorised as special receiving environment and taken into account for any release of GE trees.

In brief, where one wants to release a TREE one needs to assess the FOREST's as receiving environments, no matter how far away.

References:

FAO (2004). Preliminary review of biotechnology in forestry, including genetic modification. Forest Genetic Resources Working Paper FGR/59E. Forest Resources Development Service, Forest Resource Division. Rome, Italy.

Finstad K, Bonfils AC, Shearer W & Macdonald P (2007). Trees with novel traits in Canada: regulations and related scientific issues. Tree Genetics & Genomics 3(2): 135-139.

Katul GG, Williams, CG, Siqueira M, Poggi D, Porporato A, McCarthy H & Oren R (2006). Dispersal of transgenic conifer pollen. In Landscapes, Genomics and Transgenic Conifers. CG Williams (ed.), Springer Series on Managing Forest Ecosystems 9, Chapet 4: 121-146.

Sedjo RA (2006). Toward commercialization of genetically engineered forests: Economic and social considerations. Resources for the Future March 2006.

All references are also listed in the attached document:

Steinbrecher & Lorch: Genetically Engineered Trees and Risk Assessment – An overview of risk assessment and risk management issues. Federation of German Scientists, May 2008. Available at http://www.econexus.info/pdf/GE-Tree_FGS_2008.pdf or http://www.ifrik.org/en/gm-trees-risk-assessment

http://bch.cbd.int/cms/ui/forums/attachment.aspx?id=11

This is a reply to 889 RE: Risk assessment and risk management of specific receiving environments – with particular relevance to transgenic trees and forests [#896] - posted on 2008-12-19 11:35 by Steven Strauss

Dec 19, 2008

Dear Madam/Sir

I am a Distinguished Professor at Oregon State University and have worked and published on genetically modified trees and their risk assessment for nearly two decades. You can see most of my publications, and my CV, at this web site: http://www.cof.orst.edu/coops/tbgrc/Staff/strauss/publications.htm

I wish to respond to some of the comments made by R. Steinbrecher in a previous posting (made at 13:14 today). She attempts to suggest that GE trees as a class are substantially different from annual crops in their characteristics with respect to risk assessment and consideration of receiving environments. This is simply wrong, as explained in response to her comments below.

MY SUMMARY

In short, Norman Ellstrand and others have shown clearly that ALL agricultural crops, GE and otherwise, can pass their genes over very large distances and either establish in wild or feral environments, or mate with wild relatives and produce progeny that can grow in wild/feral places, to one degree or another, and in one place or another, around the world (for example, see his excellent book entitled 'Dangerous Liaisons,' Johns Hopkins University Press USA, 2003). This can occur via wind, insect, or animal mediated movement of pollen or seeds. In contrast to what R. Steinbrecher says, trees are not categorically different from annual crops in this respect.

The many cases of low levels of transgenes being found in wild or feral populations of annual crops, such as is very well known for creeping bentgrass in the USA, and more recently maize in Mexico, show that all GE crops will move to some degree, over quite long distances and establish in wild/feral populations. Trees therefore do not deserve special or higher stringency risk assessments due to their potential for gene flow in diverse, wild and feral receiving environments.

Instead, the questions that must be the focus of scientific risk assessments are:

1) whether the genes, given their imparted PHENOTYPES, are expected to have an effect of ecological significance ABOVE the already large impact of socially accepted agriculture and forestry practices (with their methods of intensive breeding, use of exotic species, gene flow, and agronomy/silviculture etc., and

2) if the answer to criterion 1) is yes, whether the ABUNDANCE of transgenes is likely to be high enough, in a large enough area over a long enough time, to produce a large impact compared to accepted practices and ecological fluxes in wild environments. Most of these cases of long distance gene movement produce transgenes at a very low statistical frequency (e.g., below 1%), greatly diluting any impact they would have at a distance from the source plantings. It is also unclear that any transgenes in use can provide a selective advantage of such longevity and significance in wild/feral environments, that they would continue to increase. Most transgenes are expected to only provide benefits under domesticated environments such as farms/plantations (e.g., lignin reduction or fast growth that depends

on intensive management). Even pest tolerance genes are expected to mainly have benefits in domesticated environments that favour pest proliferation, and have a limited ecological and evolutionary time span due to pest counter-evolution.

REPLIES TO STEINBRECHER

Below I respond briefly to the major comments made by R. Steinbrecher (her comments are in quotes):

"It has been well documented, that trees differ significantly from annual agricultural crops…"

As discussed above, this is simply false

"Trees have a low level of domestication"

This is true for some trees but not others. Many hybrid trees are used that are effectively sterile, and thus almost fully domesticated. There are no agricultural crop species that are full domesticated in the sense that at least some varieties cannot pass genes to feral/wild relatives in some places and cases.

"Trees have a life cycle of decades or centuries"

Of course, but domesticated trees are very often used for short rotation cycles (2-15 years is common). This allows most aspects of risk assessment to be carried out in a few years; rapid evaluation of tree varieties is common in breeding (e.g., breeding decisions are often successfully made after 2-6 years of assessment, even for trees grown for many decades in commercial plantings).

"Pollen, seed and other reproductive plant materials are dispersed over long distances"

Yes but this is also true for many annual crops, especially given the large scale of their plantings. The many cases of transgene movement from annual crops taking places over kilometers show this to be true. Also, the soil seed bank and persistence of feral relatives in annual species provide means for long term persistence of transgenes; its just a reality in trees. The question is do the phenotypic effects imparted by the genes matter ecologically or economically IN COMPARISON to accepted agricultural/forestry practices.

"Trees affect water and climate systems: forests play essential roles in managing water supply and rainfall, carbon sequestration and also climate regulation."

Yes, but it is essential to consider these effects in a broad context. Agricultural systems with annual crops, due to their large scale and annual planting and harvest cycles, are widely known to have much larger negative carbon and climate impacts than forest trees. GM trees that grow faster, are more stress tolerant, or provide economic benefits and thus favor wider planting, are likely to have far more environmental benefits than use of annual crops. Intensive risk assessment or regulatory requirements whose ultimate effect is to discourage (or preclude, as is now often the case) field research and well-developed commercial applications, are likely to do more environmental harm than good.

"Forests and woodlands, both managed and unmanaged, should thus be categorised as special receiving environment and taken into account for any release of GE trees."

As discussed above, annual crops also release genes that affect wild environments, some are woody communities and some are not. However, a major benefit with genetically modified trees (which for industrial purposes, will have transgenes of benefit under domesticated environments), is that wild forests tend to be robust, having many species and huge amounts of genetic diversity. It is thus very unclear that transgenes can have a significant effect on their adaptability or the ecological services they provide.

However, if genes are developed that really can produce some benefit to trees in the wild, if these act to increase the resilience of forest trees in the face of climate change, associated pest invasions, or other stresses that challenge their ability to survive, the net environmental benefits may very well be strongly positive, not negative. Genes for resistance to exotic pests, such as for the Chestnut Blight under development in the USA, are expected to do just this. That is, to help a species already devastated so it can recover and provide the multitude of ecological services it once did. We can expect many more exotic pests to harm forests in the future; transgenes, if tested and available in a timely manner, may provide a key tool for protection or mitigation—maybe without waiting for species devastation, as has occurred in the past. Special regulations and risk assessment requirements for trees that impede field research and commercial development is likely to do far more ecological harm than good.

This is a reply to 896 RE: Risk assessment and risk management of specific receiving environments – with particular relevance to transgenic trees and forests [#905] - posted on 2008-12-19 15:54 by Ricarda Steinbrecher

I am sure that Steven Strauss can agree that there is a fundamental difference in the requirements of a risk assessment - between an annual crop that germinates, flowers and set seed in one season, and a tree that takes years to mature before it even flowers for the first time and that then will continue to produce seed for decades, - between a crop for which outcrossing distances of 10 to hundreds of metres are discussed and trees that regularly spread seed over kilometres.

Even if the risk assessment for annual crops would be increased to take a wider dissemination and more long term effects into account, there still is a fundamental difference between the life span, the dissemination distance and the number of ecological relationships between a tree and an annual crop plant like maize.

C. Surface waters as special receiving environments [#891] - posted on 2008-12-19 08:22 by Ricarda Steinbrecher

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As Dr. Amanda Gálvez Mariscal briefly mentioned in her introduction, water also needs to be considered.

Even though LM plants are grown on land, surface waters can play a role either as a transport medium or as a medium where parts of the plant degraded and persist in a different way then on land, and where transgenic products get in contact with different organisms then on land.

Tree branches regularly get swept along by streams and get deposited along the banks where – depending on species - they can set root again.

In addition some plants rely on surface water or the sea to transport their seeds (hydrochy, drift seeds). Especially Mucuna and Dioclea species rely on rivers to disperse their seeds towards oceans and distant beaches.

Even in agricultural landscapes plant material gets deposited in surface waters (Rosi-Marshall et al. 2008). For plants producing transgenic proteins, this results possibly in a different rate of degradation and persistence in water or the aerobic and anaerobic areas of the sediment, as well as exposure of different organisms to the transgenic protein (Douville et al. 2008).

Douville et al. not only found Bt toxins from transgenic crop plants in surface water and sediment, but also observed an accumulation of transgenic Cry proteins in mussels.

First studies with the effects of Cry toxins on caddis flies (Rosi-Marshall et al. 2007) and Daphnia show that adverse effects can occur in water organisms.

Surface waters therefore need to be taken into account as a specific receiving environment.

Bøhn T, Primicerio R, Hessen DO & Traavik T (2008): Reduced Fitness of Daphnia magna Fed a Bt-Transgenic Maize Variety. Archives of Environmental Contamination and Toxicology, DOI 10.1007/s00244-008-9150-5.

Douville M., Gagné F., Andre C. & Blaise C. (2008): Occurrence of the transgenic corn cry1Ab gene in freshwater mussels (Elliptio complanata). Ecotoxicology and Environmental Safety: doi:10.1016/j.ecoenv.2008.02.006.

Rosi-Marshall et al. (2007): Toxins in transgenic crop byproducts may affect headwater stream ecosystems. PNAS 104(41): 16204-16208.

D. Risk assessment and risk management of specific receiving environment [#864] - posted on 2008-12-11 00:01 by Mr Pisey Oum

1. My name Oum Pisey, I am the Technical Advisor for Min. Environment of Cambodia and in charge in developing a biosafety and biotechnology policy. I would like to have comments on risk assessment and risk management of specific receiving environment as follows.

2. According to our guideline on RA an RM, risk assessors should conduct RA of LMOs including their environment to be released (field trial, planting, contained use, food, fee or processing). In this case, if they are to be released into the environment, they have to assess that receiving environment which include wind speed of all seasons to see how long pollen can travel, distance of planting to local plants and natural environment such as protected areas, soil ecology, water ecology, farmialr with genome of certain plant in receiving environment etc. Because fragile ecosystem can be easily susceptible to an alien species, i.e. LMOs to be released so risk assessors have to assess all of these and submit the result to decision-makers whether can decide to release into this environment.

2. Regarding RM in this case, risk assessors once they done with RA, they have to suggest approaches for managing that LMO in that specific receiving environment such as monitoring measures, emergency response measures, risk revealing to the public to be aware of and cope with it etc.

3. In developing a base line data, risk assessors should come up with the status of fragile receiving environment prior to release of a particular LMO. The status of fragile receiving environment should include land, water, air and wind speed, ground water, varieties of farm nearby and their yearly production, possible plants that can interact with that LMO once it is released into this environment, conclusion, and recommendation.

That's all I can contribute.

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Pisey Oum,

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This is a reply to 864 RE: Risk assessment and risk management of specific receiving environment [#887] - posted on 2008-12-19 08:03 by Hiroshi Yoshikura

It is important to clarify the necessity of such introduction. The LMO technology may have to be used for rescuing perishing endangered species in the centres of origin, fragile ecosystems in danger or unique ecosystem in small islands. Without such objectives, introduction of LMOs will be meaningless and sometimes harmful.

Baseline data collection should be focused on necessity of introduction of LMOs.

E. Taking into account specific regional characteristics based on agro-ecological considerations [#861] - posted on 2008-12-10 10:30 by Helmut Gaugitsch

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My name is Helmut Gaugitsch and I am head of the Department Landuse & Biosafety of the Umweltbundesamt – the Federal Environment Agency of Austria, which is the national focal point for the Cartagena Protocol. I have been working in the field of GMO risk assessment for more than 15 years.

I very much appreciate that the receiving environment is a prominent topic of this forum. Currently there is an ongoing discussion in the EU on how to consider specific environments and also protected areas in the risk assessment and the risk management of LMOs. Although within the EU there are no "megadiverse" countries in a strict sense, there is a wide range of climatic zones and therefore different biogeographic areas, which are often neglected in risk assessment studies. There are also communities of wild relatives (e.g. oilseed rape, mainly in central Europe; beet, mainly in northern Europe) of LMOs which are currently placed on the market which might be adversely affected through vertical gene-flow. I therefore want to point out, that it is of crucial importance in risk assessment of LMOs to have a close look at the receiving environment, and to include the respective data from regions in the evaluation. This also means that the applicant needs to present data from regions representing the receiving environments in order to cover the varying climatic conditions, but also the varying groups of organisms, which might be affected by the LMO. The current practice does often not fulfil this requirement.

Another point I want to raise is more focused on risk management. We have to be aware that the receiving environments are agricultural environments, which are very different depending on the agricultural tradition and economic factors in certain regions. Small scale farming and ecological farming usually lead to a higher biodiversity within the field but also in the surroundings in comparison with large scale intensive farming, which is often based on fertilizer and pesticide input. The agricultural practice and its potential to further contribute to a loss in biodiversity should also be addressed in the LMO assessment. I am well aware that in addition to agro-ecological considerations this also touches upon socio-economic issues, but the Cartagena Protocol provides for taking these issues into account.

To summarize I think that carefully studying the receiving environment, regarding its biodiversity but also the agricultural practice, is a prerequisite for a comprehensive risk assessment and consequently also for the risk management of LMOs.

This is a reply to 861 RE: Taking into account specific regional characteristics based on agro-ecological considerations [#884] - posted on 2008-12-18 18:46 by Prof. Dr. Kazuo Watanabe

As to the RA basic concept,

Receiving environment is one of major factors for RA. Consideration on Transgene x Host x Environment is the core concept.

Adaptation and invasiveness are some of contexts on environment and both textual and experimental assessments of the host species are required in the receiving environment with scientific basis.

Especially, if the host species is totally new to the receiving environment, at first the host should be carefully examined. While it is certain on any introduction of a new species to the environment, this should be carefully examined and emphasized to make sure the ecological influence.

As on many of agriculture and forest species, when the LMOs are introduced into the origin of the diversity of the species, as already discussed in many fora, further precaution is made. There shall be a more review such as OECD consensus document to add up more species with the aspects such as tree species.

Kind regards,

F. Risk assessment and risk management of specific receiving environments [#879] - posted on 2008-12-17 09:48 by Ph.D. Lúcia de Souza

From a scientific/ecological perspective, any import of any domesticated species poses a risk when introduced into a fragile ecosystem such as a small island with limited or specialized biodiversity, whether the species is transgenic or not. The risk is less, but not insignificant, if the ecosystem is robust. Thus, patches of inadvertently released imported species are often

observed in ruderal, human disturbed areas along roadsides leading from ports of entry to processing plants. Such patches usually remain limited and/or disappear with time, and do not invade agricultural or natural ecosystems.

Such historical introductions of non-transgenic material serve as an appropriate baseline for predicting whether an LMO will establish and become a problem. For example, if a country has been importing soybeans for decades, one can ascertain whether there have been established patches, and if there have been patches, whether fertile hybrids have established with indigenous species. Then, to compare transgenic glyphosate resistant soybeans to this baseline for a risk analysis, one must know from the historical evidence whether there have been problems from introduced soybeans. If glyphosate is not used along those roadsides, the risk from transgenics is no different than the past, acceptable risk. It is only when the crop itself poses a risk that one need ascertain whether the risk is greater due to the traits encoded by a transgene. In other words, special considerations for LMOs are needed only where there is a known historical risk from non-LMO introductions, and where the transgene encodes a strong selective advantage to the imported LMO.

G. Developing an approach of defining "receiving environments" [#878] - posted on 2008-12-17 09:14 by Beatrix Tappeser

The German Federal Agency for Nature Conservation has commissioned a project to develop - inter alia – a concept for defining biogeographical regions to fulfil the recommendation of taking into account the receiving environment relevant for the risk assessment of GMO as foreseen in the EU-directive 2001/18 or the Cartagena Protocol. Though it is work in progress I like to share some of the preliminary results.

...

Starting with a list of selection criteria followed by a survey of data availability, the project analysed existing biogeographical classification concepts for Europe. Any suitable regionalisation concept should appropriately reflect the specific characteristics of the faunal and floral communities of the different receiving environments of a GMP. Therefore, such a classification should be done by an ecoregion approach, meaning that different ecoregions support different organism communities that may play a different role in supporting relevant ecosystem services.

The occurrence and distribution of plant species and plant communities is well known for many parts of Europe (e.g. Ellenberg et al. 1992; Beck et al. 2005). In addition, the potential natural vegetation (PNV), i.e., the vegetation (climax stage) which would occur if there is no anthropogenic influence, has been widely mapped already (Hornsmann et al. 2008). Also much detailed information about their distribution is available for many vertebrate species such as birds (e.g., the EUNIS biodiversity database: http://eunis.eea.europa.eu/index.jsp), but for many invertebrates and in particular soil organisms such information does not exist.

The distribution of single species and the composition of organism communities are determined by local biotic and abiotic conditions. For example, the correlation between soil parameters like pH or texture and the occurrence of specific organism group compositions, which has been hypothesized for a long time (Volz 1962; Ghilarov 1965), was successfully used in recent classification concepts developed in The Netherlands (BISQ) and Germany (BBSK) (Römbke & Breure 2005). While the responsible factors vary, the same relationship has also often been found for other terrestrial invertebrates (e.g. carabid beetles: climate and vegetation (Thiele 1977).

Based on this knowledge, it is proposed to use the information about site conditions including climatic, botanical and soil parameters), which determine the composition of communities, for the classification and mapping of the distribution of terrestrial organisms. Due to their species richness, ecological relevance and – especially – their role as non-target organisms, invertebrates will be the main focus of biogeographical classification concepts to be used in the ERA of GMPs.

Realising the very different ecological requirements between and within large organism groups like plants, vertebrates and invertebrates it is likely that it will not be possible to define one classification concept for Europe which is equally relevant for all of them. However, the aim has to be to find a compromise which is as much representative as possible for all organism groups.

With the European biogeographical regions (ETC/BD 2006) there is an existing regionalisation concept applicable for epigeic organisms. For endogeic non-target organisms there is currently no suitable regionalisation concept available. For this reason it is recommended, that for the time being the cases to be separated for the ERA of a given GM crop in Europe will be identified using the European biogeographical regions.

Since the regionalisation concept is to be used in the context of the ERA of GMPs, it should be tailored for the very area in Europe where GMPs are likely to be grown. Hence, the distribution of agricultural areas in Europe should be considered. The identified 11 European biogeographical regions correspond to the different potential receiving environments for any given GMP in Europe. The overlap between these generic receiving environments and the prospective areas of cultivation for a novel GMP form the different cases, each of which should undergo a specific ERA process.

(Römpke et al. 2008)

Literature cited

Beck, L., Römbke, J., Breure, A.M., Mulder, C. (2005): Considerations for the use of ecological classification and assessment concepts in soil protection. Ecotox. Environ. Safety 62: 189-200.

Breure, A.M., Mulder, C., Römbke, J., Ruf, A. (2005): Ecological classification and assessment concepts in soil protection. Ecotox. Environ. Safety 62: 211-229.

Ellenberg, H., Weber, H.E., Düll, R., Wirth, V., Werner, W., Paulissen, D. (1992): Zeigerwerte von Pflanzen in Mitteleuropa (2nd ed.). Scripta Geobotanica 18: 1-248.

ETC/BD (European Topic Centre on Biological Diversity) (2006): The indicative Map of European Biogeographical Regions: Methodology and development. Paris, France.

Ghilarov, M. (1965): Zoologische Methoden der Bodendiagnostik. Nauka, Moskow.

Hornsmann, I., Schmidt, G., Schmidt, G., Schröder, W. (2008): Berechnung einer landschaftsökologischen Raumgliederung Europas. UWSF – Z. Umweltchem. Ökotox. 20: 25-35.

Römbke, J., Breure, A.M. (eds) (2005): Ecological soil quality - Classification and assessment. Ecotox. Environ. Safety 62: 185-308.

Thiele, H-U. (1977): Carabid beetles in their environment. A study on habitat selection by adaptations in physiology and behaviour. Springer, Berlin, Germany.

Volz, H. (1962): Beiträge zu einer pedozoologischen Standortslehre. Pedobiologia 1: 242 290.

TOPIC 5 - FLOWCHART ("ROADMAP") FOR RISK ASSESSMENT: THE NECESSARY STEPS TO CONDUCT RISK ASSESSMENT ACCORDING TO ANNEX III OF THE PROTOCOL

Introduction to the topic

by Hans Bergmans, National Institute of Public Health and the Environment (RIVM), Bilthoven, Netherlands. E-mail: Hans.Bergmans@rivm.nl

In accordance with Annex III of the Protocol, risk assessment has to be performed in a scientifically sound manner, following a sequence of steps and taking into account the relevant scientific information on a number of points to consider. The methodology reflected in Annex III is not developed 'de novo' but rather based on the experience of over 20 years of risk assessment and on the general principles as laid down in international documents such as the 1986 OECD Recombinant DNA Safety Recommendations and the 1995 UNEP International Guidelines for Safety in Modern Biotechnology.

With a view to strengthening and promoting capacity building for risk assessment as well as contributing to international harmonization, the COP-MOP decision BS-IV/11 calls for the development of "a 'roadmap', such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps, provide examples of relevant guidance documents".

This further elaboration of the Annex III of the Protocol is aimed at integrating the "Points to consider" (paragraph 9) into the steps of the risk assessment process as established (paragraph 8) by listing the former that may be relevant in the different steps, based on the existing experience with the methodology of risk assessment, whereby some points to consider have been clarified or made more explicit.

It is hoped that once the information has been integrated, the resulting flowchart will contribute to retrieving information that could be useful at the different steps and stages in the process of the risk assessment. The "Points to consider" in each step are in fact the 'crossroads' on the road map for risk assessment, where the available information that may be relevant to each of the 'crossroads' can be found. The flowchart may be used in mining data from literature databases and could help users to retrieve these

data for use in their particular circumstances and cases. As the Protocol explains, the required information may vary in nature and level of detail on case-by-case basis, depending on the living modified organism concerned, its intended use and the likely potential receiving environment.

The purpose of the discussion group "Flowchart ('Roadmap') for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol" is to collect views on how to enhance the integration of paragraph 9 of Annex III into paragraph 8, that would be taken into account by the AHTEG in the further development of this integration.

Furthermore, in this process, views and examples will be collected on how to use the flowchart as a help for information retrieval.

Suggested points for discussion

- How to combine, in a practical way, the steps in paragraph 8 and the points to consider in paragraph 9 of Annex III of the Protocol;
- Are there steps missing on paragraph 8 or do these steps cover all types of existing LMOs?
- Does paragraph 9 cover all necessary points to consider for assessing the safety of all types of existing LMOs?
- Examples of guidance materials that are useful at each of the steps listed in paragraph 8.

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Interventions

A. Welcome to the second round of discussions [#843] - posted on 2008-11-30 22:39 by Manoela Miranda

Dear Forum Participant,

Welcome to the discussion group on "Flowchart ("Roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol".

The discussions within this group will take place from 1 to 14 December 2008.

To assist in the discussions, the following is a non-exhaustive list of suggested points for discussion:

1. How to combine, in a practical way, the steps in paragraph 8 and the points to consider in paragraph 9 of Annex III of the Protocol;

2. Are there steps missing on paragraph 8 or do these steps cover all types of existing LMOs?

3. Does paragraph 9 cover all necessary points to consider for assessing the safety of all types of existing LMOs?

4. Examples of guidance materials that are useful at each of the steps listed in paragraph 8.

Also, an introduction to the topic, as well as a non-exhaustive list of suggested reading materials have been made available.

A short tutorial to assist the participants in posting messages and navigating through the Forum is available at http://bch.cbd.int/forum/tutorial_discgroup.pdf.

The CBD Secretariat thanks you for your active participation. Happy discussions!

The Biosafety Division

B. 'Roadmap' for risk assessment and risk management (3): use for retrieval of relevant information [#867] - posted on 2008-12-12 08:02 by Hans Bergmans

In a first discussion paper posted in this forum ('Flowchart or 'Roadmap' for risk assessment and risk management under the Cartagena Protocol on Biosafety') we have done a proposal for a 'roadmap' for risk assessment, that lists the steps of LMO risk assessment, and the points to consider that are relevant in each of these steps.

In a second contribution (''Roadmap' for risk assessment and risk management: information relevant to the points to consider') I have gone into the information that may be relevant at each of the points to consider.

The roadmap is presented as a linear process of steps to be taken, and points to consider that belong to each step. The points to consider at the roadmap may also be seen as crossroad from which information that has been identified as relevant can flow into the risk assessment process. In this contribution I will show one example of how this would work at a crossroad on the roadmap:

Step 1: An identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health.

The first point to consider is:

(a) The biological characteristics of the recipient organism relevant for its interaction with the likely receiving environment.

'Biology documents' for specific organisms are relevant here, as is discussed in the second contribution. Examples can be found in <http://www.oecd.org/document/51/0,3343,en_2649_34387_1889395_1_1_1_1,00.html>. By adding other available relevant information documents, we would have a comprehensive set of documents, encompassing all organisms that are currently used as receiving organisms for the construction of LMO.

This would be a first 'peg' on the crossroad, where we can 'hang' relevant information.

Clearly, filling the set of relevant biology documents will be quite some task that will probably take a lot of time and effort. Once information has been identified and added to the 'peg' on the crossroad, we should take care that this effort does not need to be repeated.

The following example shows how this may be accomplished. Information that is available on the Biosafety Information Resource Centre (BIRC) of the BCH could be analyzed for its usefulness as biology documents. When a document is found to be useful, a 'flag' could be added to its entry into the database, for instance as a keyword that indicates that it is useful at this crossroad, Step 1(a).

If all information that is relevant to step 1(a) is marked in this way, this would make it possible to retrieve, in one step, all information that is useful at this crossroad. If wanted, further keywords can be used to allow further filtering of the information, e.g. add the name of the species, so that different biology documents for one organism can be found in one step.

The same information may of course be useful at different crossroads; that would mean that it gets multiples 'flags'; this is very well possible in practice.

In the contribution on information for the points to consider I have also indicated that another type of document would be useful at the crossroad Step 1(a): documents that discuss which specific information on the biology of an organism is relevant and has to be taken into account for LMO risk assessment. This is a type of general discussion document, whereas the first type of document described above is more factual.

It would probably be useful to discriminate between these to types of documents at this crossroad: the factual documents and the discussion documents.

This could be done by creating two 'pegs', one for each type, with two 'flags' or keywords for the different types of documents. The factual documents could for instance get the keyword 'Step 1(a) biology documents', the other documents could get 'Step 1(a) discussion documents'.

In this way the information in a database like the BIRC could be very easily accessed for information that is useful for risk assessment. The main advantage would be that information that has already been found by one person and classified as useful for a certain step and crossroad on the roadmap, can be found by one push on a button by all other interested persons. In future the keywords referring to the crossroad where a document is useful can be added at the moment when a document is added to the BIRC. This would not require much extra effort. Only the addition of keywords to the already existing entries in the BIRC would be time consuming, but the result would be sufficiently rewarding.

This is a reply to 867 RE: 'Roadmap' for risk assessment and risk management (3): use for retrieval of relevant information [#895] - posted on 2008-12-19 11:17 by Helmut Gaugitsch

Dear colleagues,

my name is Helmut Gaugitsch and I work for the Austrian Federal Environment Agency. First of all I would like to stress that I regard this discussion on the flowchart/roadmap concerning the necessary steps to conduct an LMO risk assessment according to Annex III of the Protocol as very useful and interesting. This is a topic which is of a very practical nature, it affects all the risk assessors dealing with LMO risk assessment on a daily basis worldwide. We can and should learn from each other a lot!

From my point of view it is important to note that on the one hand we have accumulated some knowledge on how to do risk assessment in practice, quite some amount of guidance is available at the different levels. At the same time we still struggle with the task on how to do it in practice in a scientifically valid way. How to use the different approaches and guidance documents available? There are many open questions on how to do that and there is much room for improving, standardizing and harmonizing risk assessment.

A roadmap/flow chart may be very helpful in that respect and the discussions in this online forum and the AHTEG to be convened are crucial to make progress towards this goal.

I would like to support the detailed and thoughtful comments and suggestions by Hans Bergmans on this topic, I can agree with most of the suggestions. I would just like to add the following additional considerations:

- performing an LMO risk assessment is not an easy task and therefore I fully understand and support the complexity of the suggestions on how to integrate the points to consider (para 9 of Annex III) into the methodolog of the risk assessment (para 8 of Annex III).

- at the same time a roadmap/flowchart must be practicable and give guidance for a step-by-step procedure useful also for colleagues/institutions in the process of developing their capacity in LMO risk assessment.

- a practical instrument on how to do risk assessment in practice in my point of view has been the "matrix-approach" used by some colleagues worldwide. In this approach the 5 steps in risk assessment ("hazard identification", evaluation of likelihood, evaluation of consequences, evaluation of overall risk, risk management, summary of risk assessment including uncertainty) are performed for each introduced gene and each potential adverse effect identified in a systematic manner. Careful and precautionary analysis in a step-wise manner allows a risk assessment which did not disregard any potential risks just because they seem to be unlikely at a first glance.

- an important element in LMO risk assessment is the completeness check of a notification. Is the notified dossier complete in order to be able to perform a risk assessment? A roadmap/flowchart should also give guidance on how to perform this basic check!

- an important addition to methodology and points to consider is also the consideration of the quality of the data provided as well as the suitability of the methods with which the date have been generated. Especially in this area I see a lot of need for improvement!

- Finally another challenge is the question: Do we need criteria which are adapted to the regionally different situations? In which cases and how should they look like?

This is a reply to 895 RE: 'Roadmap' for risk assessment and risk management (3): use for retrieval of relevant information [#903] - posted on 2008-12-19 15:53 by Dr Marja Ruohonen-Lehto

Dear colleagues,

My name is Marja Ruohonen-Lehto and I work in the Finnish Environment Institute in Helsinki, Finland. Due to travelling and other obligations I am only now able to join the discussions. Again, I must state that the discussions are of high quality and very comprehensive. The description of the way forward by Dr Hans Bergmans is a good start for this important work on a flowchart/roadmap. Further, I very much appreciate the comments and additions made by Dr Helmut Gaugitch. He raises very pertinent issues in risk assessment that we still have to work on: we must emphasize and set scientifically sound criteria for the quality of data (see e.g. publications by Michelle Marvier and Peter Kareiva) and suitability of methods used and to be used for e.g. data collection must be further evaluated. Statistical power of the gathered/existing data is a very important issue.

Moreover, the 5 step approach of risk assessment that Dr Gaugitch refers to in his comment is very much in line with the Protocol approach to risk assessment and risk management

We certainly have a lot of experience on some aspects and applications of biotechnology but there is clear lack of data and information on certain, more recent applications. This must be kept in mind and lack of data must be approached in a scientifically sound way.

C. Flowchart for Risk Assessment [#888] - posted on 2008-12-19 08:11 by Hiroshi Yoshikura

General Comment

In some cases, LMOs might be released into the environment so that they persist there, for example, when LMO technology is applied to rescue perishing endangered species. Annex III should recognize potential of such applications.

Specific comments

1. It is important to incorporate or recapitulate the general principle paragraph 5, i.e, "Risks associated with living modified organisms or products thereof, namely, processed materials that are of living modified organism origin, containing detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology, should be considered in the context of the risks posed by the non-modified recipients or parental organisms in the likely potential receiving environment." in sections of methodology (paragraph 8) and Points to consider (paragraph 9).

2. Under Methodology, it is important to identify "the non-modified recipients or parental organisms" and "the environment where the non-modified recipients or parental organisms normally exist", which may be called "conventional counterpart(s)" and "original/conventional environment", respectively. With such comparators, points described in paragraphs 8 and 9 can be properly assessed.

3. It is important to note that all the considerations from (a) to (f) apply to the conventional counterparts, i.e., the non-modified recipients or parental organisms.

For Methodology

1) The first step could be to ask whether the non-modified recipients or parental organisms are alien to the receiving environment.

2) If they are, they can be examined by using conventional law, such as quarantine law, and then for their possible familiarity to the potential receiving environment. Familiarity can be assessed by asking whether we have sufficient knowledge to manage them once they are introduced into the environment

3) Then, new or altered hazard (the definition of hazard used here is "a biological agent with the potential to cause an adverse effect", codex definition) of the LMO in question should be identified through safety assessment using the non-modified recipients or parental organisms as comparators.

4) The assessment process (a – f) and results, including the scientific data and information used for assessment, should be recorded.

5) Monitoring

The term "monitoring" in (f), needs further consideration. The interaction of LMOs with other organisms and environment is complex, and just monitoring the survival of LMOs in the environment is often meaningless. Therefore, when monitoring is considered, "its need and utility should be considered, on a case-by-case basis, during risk assessment and its practicability should be considered during the risk management. The monitoring may be undertaken for the purpose of:

a) verifying conclusions about the absence or possible occurrence, impact and significance of potential environmental effects,; and

b) monitoring changes in environmental parameters (that are identified through the risk assessment) to determine their environmental impact. "

Note

1. The sentence in the quotation mark is modified (underlined part) from paragraph 20 of Principles for the Risk Analysis of Foods Derived from Modern Biotechnology.

2. The monitoring of GM food and LMO may appear entirely different in nature. However, the principle could be similar. Differently from chemicals used for food additives, safety of whole food, such as GM potatoes, rice, etc, is very difficult to evaluate on account of interaction with other foods, physiological condition of consumers, cooking, storage, consumption pattern, etc. Under these circumstances, comparative safety assessment approach is adopted (paragraphs 9-13 of Guideline for rNDA foods).

3. Monitoring GM food is not easy to practice and is very costly. Therefore, it was recognized that, if monitoring is to be performed, it is important to have a hypothesis to prove. The situation could be the same for LMOs released into the environment. Without knowing what to prove, we do not know what events to be followed.

In some case, monitoring survival of LMOs per se may not be important, but its adverse or beneficial effects should be monitored. In this respect, "biomarkers or other parameters for monitoring the environmental effects of LMOs should be identified if there are any. "

D. Drawing a Roadmap [#847] - posted on 2008-12-02 12:13 by Piet van der Meer

Dear All,

My name is Piet van der Meer. I have been working in the field of biosafety since 1986, the first 13 years for the Dutch Government and the last 9 years providing support to Governments and various international organizations, among which the Public Research and Regulation Initiative (PRRI).

As with the on line discussion on capacity building, I found the previous discussions on risk assessment for GM trees, GM fish, Pharmaplants and GM micro-organisms a fascinating exercise.

Picking up from the debate under those previous discussions, I post the following general thoughts for your consideration and feedback.

As the background document produced by Hans Bergmans reminds us, the general principles and methodology of risk assessment as outlined in Annex III of the CPB are scientifically sound and based on the experience of over 2 decades of risk assessment.

Those general principles and methodology have shown to be adequate for GM crop plants with altered agronomic traits, and they are equally valid and appropriate for risk assessment for relatively new cases, such as GM trees, pharmaplants, GM fish and GM micro-organisms. As with GM crop plants with altered agronomic traits, practical guidance how to apply this methodology in these specific areas will certainly be useful.

However, the fact that additional guidance may be useful should not be interpreted as that for those cases adequate risk assessments cannot be done. This is a misperception. The methodology of Annex III can be applied, also where there are areas of uncertainty. As the Protocol explains in Annex III: "Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment.

What the previous on line discussions on RA also showed is that in conducting risk assessment we do not look at the GMOs "in a vacuum". As we can see from Annex III of the Protocol, a key characteristic of risk assessment is that it is comparative. Risk assessment follows a number of steps and comparisons are made in the subsequent steps of the risk assessment.

Reading some of the postings of the previous on line discussions, I realized that we need to discuss further that the nature of these comparisons is different for each step, and by consequence, the "comparator" we choose can be different for each step. This is why for example the EFSA guidelines refer to the "appropriate comparator".

The first step of the risk assessment as outlined in Annex III, is to identify whether there are any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects.

The first question here is therefore which novel characteristics result from the genetic modification. Here we typically make a distinction between intended changes (e.g. the genes inserted) and possible unintended changes.

To identify whether there are any unintended changes, we compare some key characteristics with the characteristics non-modified host organism. For plants, often a near isogenic line is used for this first comparison. Once a "change" from the non-modified host is observed, we ask ourselves whether that change is within the normal variation of that species. Differences from a near isogenic line do not mean there is a concern, since each species is normally quite variable.

The next step in the risk assessment is to identify any of the identified changes may have an adverse effect.

As was explained in one of the postings in the previous discussions, this step is tied to what we call the "problem formulation", which in turn is related to protection goals. I hope we can discuss this further too.

(NB: It is important to remain aware that a "change" in itself is not 'risk'. It only means "change". We should remember that in conventional plant breeding, there are typically many unintended changes observed, many of which are not desired by the plant breeder and therefore thrown away, and some are actually of interest to plant breeders and kept for further development.)

In the next step of the risk assessment we evaluate the likelihood of the potential adverse effects being realized.

This is followed by an assessment of the consequences should these adverse effects be realized. In this step we make again a comparison, this time to see whether a certain effect on biodiversity would be significant. Significance here is to be seen in the context of the protection goals and natural fluctuations, which brings us back to the "problem formulation".

Next follows An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized.

And finally we move to the last step of the risk assessment in Annex III, i.e. we ask ourselves whether or not the identified risks – if any - are acceptable or manageable.

In evaluating whether identified risks are acceptable, we have again a comparison step. This time we make a comparison between an identified risk associated with the GMO with the risks posed by the non-modified recipients and their use.

As this sequence shows, in the different steps of the risk assessment we make different comparisons, taking into account different parameters.

As I often explain in RA training workshops, the methodology of risk assessment is in a way similar to a recipe for baking a cake. (I say "in a way" to avoid the suggestion that risk assessment is a piece of (baking a) cake). A recipe tells us to follow a number of steps and which ingredients to use at which steps. The same is the case for risk assessment, annex III tells us in paragraph 8 which steps to follow and in paragraph 9 which ingredients to use.

I therefore very much support the suggestion Hans Bergmans made in the back ground document that in assisting the development of the 'roadmap' for risk assessment MOP4 has asked for, we identify which points to consider mentioned in paragraph 9 of Annex III can be of relevance in which steps mentioned in paragraph 8 of Annex III.

(edited on 2008-12-02 13:13 by Piet van der Meer)

This is a reply to 847 RE: drawing a Roadmap [#885] - posted on 2008-12-18 18:51 by Prof. Dr. Kazuo Watanabe

This is more to follow up on the comments by Dr. Piet van der Meer, my historical colleague since the negotiation of the Protocol.

The Roadmap is like a blueprint without a building at the beginning when starting RA. But now we have a lot of field release of LMOs-FFP. With the feedback of the experiences, there could be extension and elaboration on tow ways.

One for elaborating on different categories of LMOs for further tune-up to facilitate efficiency and efficacy of RA.

Another could be future outlet of the experiences reflected to the simplification or more details tuning of the direction.

Kind regards,

E. Cuba´s opinion in relation to the topic Flowchart ("Roadmap") for risk assessment [#871] - posted on 2008-12-12 15:48 by Leticia Pastor Chirino

Dear colleagues,

Please, I would like to express Cuba´s opinion in relation to the topic Flowchart ("Roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol.

In the case of Cuba, the risk assessment process on LMOs is envisaged as a part of the decision making process. The information to be submitted by the applicants, according to the specific activity to be performed is detailed in five annexes of the legal instrument that put in place this administrative process (Resolution No. 180/2007, is posted on the BCH). The risk assessment process is undertaken following a Guide on risk assessment and risk management elaborated with such purpose. The revision of the dossier is carried out by using a check list included in the mentioned guide which also establishes the different stages to be follow for the performing of a RA process.

These stages are the followings:

1. Definition of the relevant adverse effects.
2. Identification of hazard, using qualitative techniques.
3. Evaluation of the possibility of the occurrence of each identified hazard.
4. Evaluation of the consequence.
5. General estimation of the risk for each identified hazard.
6. Analysis of the uncertainty.
7. Parameters of acceptability of risks.

this guide will be post on the BCH shortly.

Best regards

Dra. Leticia Pastor Chirino.

National Centre for Biosafety. Cuba.

F 'Roadmap' for risk assessment and risk management (2): information relevant to the points to consider [#866] - posted on 2008-12-12 03:10 by Hans Bergmans

The concept of a 'roadmap' for risk assessment and risk management is explained in the posted contribution ''Roadmap' for risk assessment and risk management under the Cartagena Protocol on Biosafety'.

One of the advantages of the roadmap is that it can be used as a framework for making clear what information is necessary for performing the different steps of a risk assessment.

This contribution discusses the type of information that is necessary and useful for the different points to consider in the steps of the risk assessment process, and provides some examples.

In order for the roadmap to function properly as a framework for information, the referenced information should be comprehensive. As a matter of fact, it should be possible in principle to indicate for all literature references in a database like the Biosafety Information Resource Centre (BIRC) of the BCH where the information comes in usefulness within the framework of the roadmap.

I would ask you and encourage you to provide further discussion on and examples of information that could be added at the different points to consider of each step. This subject is also on the agenda to be taken on board by the forthcoming AHTEGs, for further development.

The roadmap itself is presented here in 'shorthand', with shortened headings for the steps and point to consider. Please refer to the first posted document on the road map for full explanation.

Roadmap for risk assessment and risk management: useful information

Step 1: Identification of novel genotypic and phenotypic characteristics associated with the LMO.

Points to consider:

(a) The biological characteristics of the recipient organism.

The (potential adverse) effects that an LMO can have on the environment are to a large extent determined by the biological properties of the non-modified recipient organism. This type of information has been published for number of organisms in 'biology documents', e.g. the OECD consensus documents <http://www.oecd.org/document/51/0,3343,en_2649_34387_1889395_1_1_1_1,00.html>), for instance the document for Zea mays <http://www.olis.oecd.org/olis/2003doc.nsf/LinkTo/env-jm-mono(2003)11>.

Not all information that is available on the biology of plants will be relevant for the specific purpose of step 1. What type of information is particularly useful in biology documents may be further discussed, as is done in the OECD 'points to consider' document <http://www.olis.oecd.org/olis/2006doc.nsf/LinkTo/NT00000B8E/$FILE/JT03206674.PDF> .

(b) Characteristics of the vector.

Usually this is very case specific information, and information can be found in the information submitted by applicants. The choice of vector will also depend on the type of transformation procedure that is used (A. tumefaciens mediated transformation, biolistics), and general information on these techniques may come in useful here.

(c) Characterization of the insert(s): gene products, level of expression, function, physiological effect on the recipient organism.

What would be needed for characterization of the gene product and its physiological effect on the recipient organism are overview papers on the information that is relevant to the risk assessment of the gene products. This type of compilation is available for some traits that have been used, or are going to be used, in LMOs. We find that this kind of overview is less easily available than the 'biology documents' mentioned in paragraph (a) of this section.

Examples are: the OECD report on the biosafety of Bt protein expressed in plants <http://www.olis.oecd.org/olis/2007doc.nsf/LinkTo/NT00002DF6/>, and a report on drought tolerance and on expression of omega-3 fatty acids, made available on the BIRC <http://bch.cbd.int/database/attachedfile.aspx?id=1904>.

Requirements for detailed characterization, e.g. molecular characterization and characterization of levels of expression, are set by competent authorities, e.g. a document on molecular characterization <http://www.aphis.usda.gov/brs/canadian/usda03e.pdf> that has been agreed upon by the US and Canada.

(d) Relevant biological characteristics of the donor organism(s).

This information differs from the information on the trait of the donor organism that has been introduced into the receiving organism (i.e. the information mentioned in paragraph (c) of this section), in that the activity of the trait in the donor organism may provide insight into what could be happening in the LMO.

Differences between the situation in the donor organism and in the LMO may also be important. An example would be the case of Bt toxin: the toxin is expressed in the donor organism as an inactive protein, that has to be activated by proteolytic cleavage. In the LMO it is expressed as a truncated protein that is immediately active as toxin. This has to be kept in mind when the potential effects of the LMO (with truncated toxin) are compared to the effects of the donor (with its full length protein, that has to be activated for toxicity).

(e) Characterization of the resulting LMO

The actual characterization of the phenotype of the LMO, is based on the characterization of the insert in paragraph (c) in this section.

The characterization is done on a case by case basis. General guidelines are available from bodies performing risk assessment, e.g. the EFSA guidance document < http://www.efsa.europa.eu/cs/BlobServer/Scientific_Document/gmo_guidance_gm_plants_en,0.pdf?ssbinary=true>

Practical examples may be found in the summaries of risk assessments for specific LMOs, publishes on the BCH, depending on the level of detail of the summaries.

(f) Conclusions regarding significant intended and unintended changes in the LMO.

This conclusion is a summary of the considerations in (a) – (e) in this section, and is the basis for the considerations in the next steps. Clearly, the conclusions have to be drawn on a case by case basis. The changes are characterized by a comparative approach, comparing the LMO and its use to the relevant counterpart. This is generally explained in the guidance document mentioned in paragraph (e) of this section.

Step 2: Evaluation of the likelihood of these adverse effects being realized.

Points consider

(a) Information relating to the intended use of the LMO.

This information is provided on a case by case basis by the applicant.

(b) Likely receiving environment.

Characterization of the likely receiving environment will be the local environment of the risk assessor. The risk assessor, or by experts directly available to the risk assessor, e.g. local environmental or agricultural extension services, are therefore in the best position to do this characterization. It would be useful to make available lists of extension services, or actual examples of characterization of the receiving environment for purposes of LMO risk assessment, as examples.

Step 3: An evaluation of the consequences should these adverse effects be realized;

Points to consider

(a) Characteristics of the likely potential receiving environment, and of experience with similar consequences of traditional practices, as a baseline.

The use of baseline information is very important, for the comparative approach that is a principle of LMO risk assessment. The comparative approach has been described, e.g. in the EFSA guidance document referred to in Step 1, e.

Step 4: An estimation of the overall risk posed by the LMO.

The result of this step follows from the steps 1 – 3, on a case by case basis.

General guidance on this topic will be available for different legislative frameworks (e.g. the EFSA guidance referred to in Step 1, e).

Practical examples may be found in the summaries of risk assessments for specific LMOs, publishes on the BCH, depending on the level of detail of the summaries.

Step 5: A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks;

Points consider

With regard to acceptability of identified risks:

(a) Likely receiving environment and experience with similar consequences of traditional practices, as a baseline.

(b) Evaluation of the risk associated with the LMO in the context of the risks posed by the non-modified recipients in the likely potential receiving environment.

For both (a) and (b) baseline data are needed. Examples of the need for baseline data for a specific case, and of the discussion on the interpretation of baseline data, can be found in the previous discussion forum, on the topic of transgenic trees,

With regard to manageability of identified risks:

(c) Relevant management practices that are in use for the non-modified recipients, or for other organisms that require comparable risk management.

Examples of risk management practices are provided in Annex 5 of the 1995 UNEP International Guidelines for Safety in Modern Biotechnology <link http://www.unep.org/biosafety/Documents/Techguidelines.pdf>. Identification of similar guidance material would be useful.

(d) Relevant methods for detection and identification of the LMO and their specificity, sensitivity and reliability.

One example of a document that is relevant, in this case for micro-organisms introduced into the environment, can be found at <http://www.olis.oecd.org/olis/2004doc.nsf/LinkTo/NT0000A48A/$FILE/JT00166030.PDF >

Identification of similar guidance for higher organisms would be useful.

Step 6: Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment.

The Precautionary Principle of the Rio Declaration (principle 15 in <http://www.unep.org/Documents.multilingual/Default.asp?DocumentID=78&ArticleID=1163> is an important instrument for decision making in case of scientific uncertainty.

See also a Communication by the Commission of the EU COM(2000) 1 <http://ec.europa.eu/dgs/health_consumer/library/pub/pub07_en.pdf > for a general discussion on how to use the precautionary principle in environmental safety.

G. Flowchart or 'Roadmap' for risk assessment and risk management under the Cartagena Protocol on Biosafety (1) [#865] - posted on 2008-12-12 03:08 by Hans Bergmans

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The terms 'flowchart' or 'roadmaps' are used in several documents of COPMOP, and in the terms of reference for the AHTEGs that will be organized before the next COPMOP. But what is meant by these terms?

We have agreed that under the Protocol, risk assessment of LMOs is done in accordance with Annex III <http://bch.cbd.int/protocol/text/article.shtml?a=cpb-43> of the Protocol. There are two paragraphs in Annex III that are crucial for how to actually perform such a risk assessment: paragraphs 8 and 9, under the heading 'methodology'.

Paragraph 8 specifies the steps of risk assessment, paragraph 9 specifies the points that have to be taken into consideration during risk assessment.

It is good to realize, as is also indicated in the introduction to this topic, that the methodology reflected in Annex III was not developed 'de novo' but rather it is based on the experience of over 20 years of risk assessment and on the general principles as laid down several documents of international organizations (for examples refer to the Introduction to this topic).

The 'flowchart' or 'roadmap' (I will further use the term 'roadmap') provides an integration of the steps and the points to consider of paragraphs 8 and 9, to show how to proceed from step to step in the risk assessment process. Points to consider are allocated to the steps where they are relevant. The importance of having a roadmap is to know and agree on what points need to be taken into account in the different steps.

In this way the roadmap can strengthen capacity building for risk assessment as well as contributing to international harmonization.

I present here an example for further discussion, of how we see that the roadmap could be set up.

The roadmap lists the points to consider that may be relevant in the different steps, based on the existing experience with the methodology of risk assessment, whereby some points to consider have been added (points to consider derived from paragraph 9 of Annex III are indicated as such).

For taking into account each point to consider in the road map, information is needed that is relevant for each point. In another contribution to the discussion I intend to show what type of information we think is relevant at each point to consider. In a third contribution I will try to make clear how the points to consider in each step can function in practice as 'cross roads' on the road map. These 'crossroads can help to make the information that is available in databases like the Biosafety Information Resource Centre (BIRC) of the BCH, easier accessible.

Proposal for the Roadmap for risk assessment and risk management under the Cartagena Protocol on Biosafety

Step 1: An identification of any novel genotypic and phenotypic characteristics associated with the LMO that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health.

Points to consider:

(a) The biological characteristics of the recipient organism (e.g. its taxonomic status, its origin, centres of origin and centres of genetic diversity, and a description of the habitat where the organisms may persist or proliferate) relevant for its interaction with the likely receiving environment (Annex III, 9a).
(b) Characteristics of the vector (its identity, and its source or origin, and its host range) if used, and in as far as present in the LMO (Annex III, 9c).
(c) Characterization of the insert(s), including, as appropriate, the gene products, their level of expression, their function and physiological effect on the recipient (Annex III, 9d).
(d) The biological characteristics of the donor organism(s) relevant for the characterization of the donor gene(s) and its genotypic and phenotypic effects in the recipient (Annex III, 9b).
(e) Characterization of the resulting LMO, with a focus on identifying differences in biological characteristics between the LMO and those of the recipient organism (Annex III, 9e).
(f) Conclusions regarding the living modified organism, and the differences between the biological characteristics of the living modified organism and those of the recipient organism.

Step 2: An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the LMO.

Points consider:

(a) (a) Information relating to the intended use of the LMO (e.g. confined field trial, or unconfined large scale cultivation) (Annex III, 9g).
(b) (b) Likely potential receiving environment: information on the relevant characteristics (e.g. geographical, climatic and ecological characteristics) of the likely potential receiving environment (Annex III, 9h).

Step 3: An evaluation of the consequences should these adverse effects be realized.

Points to consider:

(a) Characteristics of the likely potential receiving environment (Annex III, 9h), and of experience with similar consequences of traditional practices (e.g. agricultural practices, pest management) as a baseline.

Step 4: An estimation of the overall risk posed by the LMO based on the evaluation of the likelihood and consequences of the identified adverse effects being realized.

Step 5: A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks.

Points consider:

With regard to acceptability of identified risks:

(a) (a) Likely potential receiving environment (Annex III, 9h), and experience with similar consequences of traditional practices, as a baseline.
(b) (b) Evaluation of the risk associated with the LMO in the context of the risks posed by the non-modified recipients in the likely potential receiving environment (Annex III, 9e).

With regard to manageability of identified risks:

(c) (c) Relevant management practices that are in use for the non-modified recipients, or for other organisms that require comparable risk management.
(d) (d) Relevant methods for detection and identification of the LMO and their specificity, sensitivity and reliability (Annex III, 9f).

Step 6: Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment.

H. Flow chart for risk assessment - taking into account specific environments, biodiversity richness, protected areas and agroecosystems. [#863] - posted on 2008-12-10 15:58 by Dr Eliana Fontes

In discussing the topic of risk assessment requirements for specific environments, I appreciate the overview prepared by Dr Helmut Gaugitsch on the issue of potential long-term effects of LMOs released into the environment, as it points out the challenges and the opportunities of the post-release monitoring as a possible additional mechanism to address the safe use of GMOs. This is because GMOs are going to be introduced in a variety of environments, each with specific and relevant characteristics that may be taken into account. I have been carefully following the discussions around the new technologies and the conditions for their safe application, taking into account the case of Brazil. Although only cassava among the main food crops was domesticated in Brazil, the country is centre of origin of many wild relative and land races of other cultivated species such as rice, cotton, potatoes, and beans. In addition to this, and to the rich biodiversity present in the country, the Brazilian territory ranges from 5 degrees of Latitude North to ca. 32 degrees of Latitude South, i.e., the environment is widely diverse and have many specific climate and soil characteristics, and a web of big rivers connected among themselves by streams, channels and floods. Our environmental law requires that the Gallery Forests (semi deciduous vegetation that surround rivers and springs) inside the farmers are preserved and that 50% of each farm area is not cultivated, but kept with natural vegetation to protect biodiversity. All this variety and diversity is yet little known. And yet, some field trials of transgenic Eucalyptus are already under way in the country, and for these GMOs, many risk hypotheses can only be tested under field conditions and over a time that can be considered long when compared with transgenic crops. So in my view, and based on the excellent contributions given in the different discussion forums, many knowledge gaps still exist in specific environments, not only in Brazil but in many other countries, particularly in the tropical and subtropical range of the world. I wish we could discuss this issue in the context of designing a flowchart for risk assessment based on annex III of the Protocol.

(edited on 2008-12-10 16:00 by Dr Eliana Fontes)

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