SOUTH ASIA
BIOSAFETY PROGRAM

November 2007
Vol.3 No.11

NEWSLETTER

for private circulation only - not for sale

www.agbios.com/sabp

SABP

The South Asia Biosafety Program (SABP) is an international developmental program initiated with support from the United States Agency for International Development (USAID). The program is implemented in India and Bangladesh and aims to work with the local governments to facilitate implementation of transparent, efficient and responsive regulatory frameworks that ensure the safety of new foods and feeds, and protect the environment.

SABP is working with its in-country partners to:

- Identify and respond to technical training needs for food, feed and environmental safety assessment.
- Develop a sustainable network of trained, authoritative local experts to communicate both the benefits and the concerns associated with new agricultural biotechnologies to farmers and other stakeholder groups.
- Raise the profile of biotechnology and biosafety on the policy agenda within India and address policy issues within the overall context of economic development, international trade, environmental safety and sustainability.

SCIENTIFIC RATIONALE FOR REGULATING PLANT BIOTECHNOLOGICAL PRODUCTS CONTAINING TWO OR MORE TRAITS (STACKED GENES)

K.K. Tripathi, Adviser/Scientist 'G', Department of Biotechnology, Ministry of Science & Technology

Stacked gene products can be produced through three different approaches:

1. Traditional breeding and selection of two plant varieties, each of which contains one or more previously inserted transgenes;
2. the insertion of an additional transgene by transformation of a plant already improved by plant biotechnology; or
3. the insertion of multiple genes and traits into a non-transgenic plant via a single transformation event.

The regulatory process for plants produced by any of the three approaches is similar.

Regardless of the method used, plants with transgenic traits can be crossed with either non-transgenic or other transgenic plants using methods that are the basis for traditional plant breeding. The stacked gene products derived by traditional plant breeding are phenotypically indistinguishable from plants containing multiple traits as the result of a single transformation event or multiple successive transformation events. Whereas plants containing multiple genes at a single insertion site or genetic locus provide increased efficiencies from a plant breeding perspective, the production of plants that express desired traits for each of multiple, independent genes at a single insertion site in the same plant becomes increasingly difficult with current techniques of gene insertion. Therefore, combinations of these processes will likely be employed to achieve multiple traits in a single plant. To date there are a limited number of genes that have been introduced into commercially available transgenic plants however, latterly, hundreds of potential stacked gene product combinations are possible from these single transgenic products.

Safety assessment of stacked gene products:

Based on scientific principles and the experience with traditionally bred crops, from a food, feed and environmental safety perspective the conclusions of the assessments conducted on each of the independent, single gene products should also apply to the combined stacked gene products, except where there is a reasonable mechanism for the combined traits to interact or target the same metabolic pathway. The World Health Organization (WHO) confirmed the conclusion that crossing two varieties that were independently generated and shown to be substantially equivalent to traditional varieties would, when crossed by conventional plant breeding techniques, be expected to be substantially equivalent to the parents. The concept of substantial equivalence, as described by WHO, includes the concept that once a genetically modified plant variety is deemed to be as safe as conventional plant varieties the new traits become part of the point of reference for the safety assessment of future products. Where the combination of two traits might be expected to have an interactive effect, then additional safety information on the specific stacked gene product would be warranted. Under these circumstances, the developer would need to perform detailed characterisation of the stacked gene product to assure that the desired effect was achieved and that no unpredicted effects resulted. Since unintentional as well as intentional food, feed and/or environmental effects are evaluated for each trait independently during the safety assessment and regulatory approval processes, only combinations of traits that produce an unexpected interactive or synergistic effect warrant additional safety assessment of the stacked gene product. Furthermore, the additional safety assessment should focus on the targeted metabolic or biosynthetic pathway(s).

The combination of traits warranting additional safety assessment can be divided into three categories:

- Category 1: Unrelated traits (*e.g.*, insect protection and herbicide tolerance; male sterility and virus resistance; insect protection and food quality improvement, *etc.*).
- Category 2: Related traits, but involving different pathways or distinct modes-of-action (*e.g.*, glyphosate herbicide tolerance and glufosinate herbicide tolerance; multiple proteins with different modes-of-action that provide insect protection, *etc.*).
- Category 3: Related traits functioning in the same metabolic or biosynthesis pathway (*e.g.*, two enzymes involved in starch biosynthesis or lipid biosynthesis).

In Categories 1 and 2 there is no information or experience to indicate that the combination of these traits would raise any new food, feed or environmental safety issues because each of the genes function independently. If both products were independently shown to be "as safe as" other commer-

(continued on page 2 - see Stacked Genes)

THE CALENDAR

CALENDAR OF EVENTS

INDIA

Event	Organization	Date	Place
Practical and Theoretical Course on "Insecticidal Proteins: Application and Regulatory Issues"	International Centre for Genetic Engineering and Biotechnology (ICGEB)	November 12 - 23, 2007	New Delhi
Biotech-2007: 5th Annual Conference of Biotechnology Society of India	Industrial Toxicology Research Centre (ITRC)	November 17 - 19, 2007	ITRC, Lucknow
National Orientation Course on Biosafety Considerations for Evaluation of Transgenic Crops	National Bureau of Plant Genetic Resources (NBPGR) (for more information go to http://www.nbpgr.ernet.in/PDF/Brochur_biosafety_2007.pdf)	November 27 - December 4, 2007	NBPGR, Pusa Campus, New Delhi
Commercialization of Biotechnology	Biotech Consortium India Limited (BCIL) and Department of Biotechnology (DBT)	November 27, 2007	National Agricultural Science Centre (NASC) Complex, New Delhi
Entrepreneurs Development Programme in Biotechnology	DBT and BCIL	December 3 - 6, 2007	Agartala
Farmers Awareness Workshops on Benefits of GM Crops	BCIL and All India Crop Biotechnology Association (AICBA)	November – December 2007	Tamil Nadu, Andhra Pradesh and Haryana
Consultation on Herbicide Tolerant Crops	National Research Centre on Weed Science, BCIL and AICBA	December 10 - 11, 2007	New Delhi
Workshop on Regulatory Compliance for Field Trials	BCIL and AICBA	December, 2007	

Stacked Genes - *continued from page 1*

cial crop varieties, then the combination of the two traits by conventional breeding techniques would raise no new safety concerns and hence warrant no additional safety evaluation of the stacked gene product. This process would be no different than combining conventional traits using traditional plant breeding techniques.

Products in Category 3 could raise some specific additional food/feed safety questions, especially pertaining to the composition of the final products. In fact, for many of these products, only the final combination of traits may produce the desired product of commercial interest. That is, the desired effect may require the combination of inserted genes. For these products, additional composition information that specifically addresses the pathway(s) under question to assess any impact on the types and/or amounts of compounds produced in those pathway(s) would be appropriate. It might also be appropriate to assess the nutritional performance of a stacked trait product designed for improved nutritional attributes. For example, there are stacked gene products under development that result in interactive or synergistic modifications of the fatty acid composition of corn (*e.g.*, increased oleic acid and increased stearic acid) that would, even if created by the traditional breeding process, warrant additional assessment of the resulting fatty acid types and levels.

CURRENT REGULATORY PARADIGMS ON STACKED GENE PRODUCTS:

The Indian regulatory system has issued guidelines for the biosafety evaluation of transgenic plants with single as well as stacked genes. The guidelines can be accessed at www.igmoris.nic.in and http://dbtbiosafety.nic.in.

When a transgenic variety is developed and released based on a cassette comprising given promoter(s) and gene(s) following all the necessary biosafety and agronomic trials, the further derivatives of this variety or its immediate transgenic parent can be released upon evaluation of one / two-year agronomic performance trials under the All India Coordinated Crop Improvement Project (AICCIP) system and by the applicant. The necessary permission for release is granted by the Genetic Engineering Approval Committee (GEAC) upon examination of the relevant data submitted to it by AICCIP and the applicant.

The United States Food and Drug Administration (FDA) and Food Standards Australia New Zealand (FSANZ) require no additional food, feed or environmental safety data for stacked gene products on which the regulatory process has been completed for the single trait products. The Japanese Ministry of Health, Labour and Welfare has issued similar guidance for stacked gene products with no regulatory

(continued on page 4 - see Stacked Genes)

SPOTLIGHT ON THE WORDWIDE WEB

Over the next number of newsletters we will be spotlighting some important websites, created by the Department of Biotechnology (DBT) and the Ministry of Environment and Forests (MoEF), that provide information on GMOs.

This month we feature the **Department of Biotechnology Indian Biosafety Rules & Regulations** (http://dbtbiosafety.nic.in). In the months ahead we will look at the websites of the Ministry of Environment and Forests, Government of India; Capacity Building on Biosafety; India Biosafety Clearing House; National Research Centre on Plant Biotechnology; Department of Agriculture and Cooperation, Ministry of Agriculture, Government of India; and Biotech Consortium India Limited (BCIL). - Editor

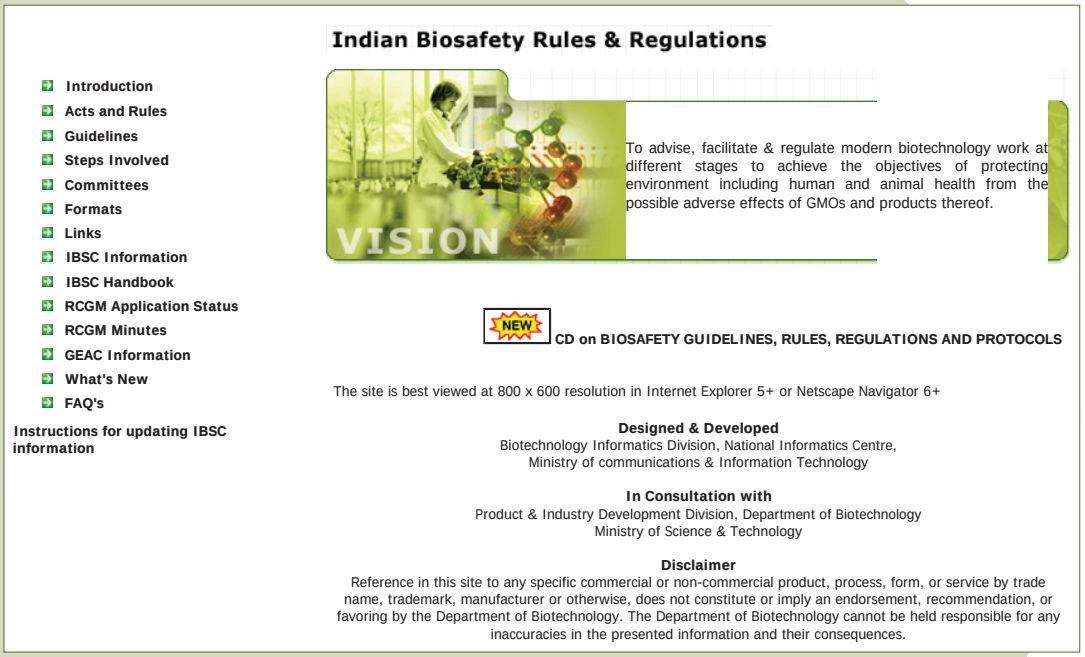
SPOTLIGHT ON THE WORLDWIDE WEB

Department of Biotechnology Indian Biosafety Rules & Regulations

(http://dbtbiosafety.nic.in)

Modern biotechnology (recombinant DNA technology) is recognized as having great potential for the promotion of human well being, particularly in meeting critical needs for food, agriculture and healthcare. Biosafety refers to the need to protect the environment including human and animal health from the possible adverse effects of the genetically modified organisms (GMOs) and products thereof derived from the use of modern biotechnology. Biosafety also refers to promoting safe laboratory practices, procedures, proper use of containment equipment and facilities, risk assessment and risk management, evaluation of GMOs, *etc*. Biosafety regulations are to facilitate and regulate use of modern biotechnology work at different stages to achieve the objectives of biosafety.

For facilitating and regulating the research work on GMOs and products thereof on a laboratory scale and also in commercial applications, the Government of India has notified "Rules for the Manufacture/Use/Import/Export and Storage of Hazardous Microorganisms, Genetically Engineered Organisms or Cells" through Notification No. G.S.R.1037(E), dated December 5, 1989 under the provisions of Environment (Protection) Act, 1986 through the Ministry of Environment and Forests (MoEF). These rules are commonly referred to as 'Rules 1989'. The two main agencies identified for implementation of the Rules 1989 are the MoEF and the Department of Biotechnology (DBT), Ministry of Science and Technology, Government of India. The Rules 1989 have also defined Competent Authorities and the composition of such authorities to handle the various aspects of biosafety.



To implement the Rules 1989, DBT has brought out guidelines from time to time. In 1990, the guidelines under the title "Recombinant DNA Safety Guidelines" were published. These guidelines provide information to researchers on the Rules, implementation of the provisions of the Rules, approval mechanisms, risk groups, handling of GMOs, import of GMOs, *etc*. In 1998, DBT published guidelines under the title "Revised Guidelines for Research in Transgenic Plants and Guidelines for Toxicity and Allergenicity Evaluation of Transgenic Seeds, Plants and Plant Parts". These Guidelines provide information on the level of approvals for conducting research in transgenic plants, category of experiments and testing procedures for toxicity and allergenicity, *etc*. In 1999 DBT also brought out guidelines for "Generating Pre-clinical and Clinical Data for r-DNA based Vaccines, Diagnostics and Other Biologicals". From time to time, DBT is devising proformas for submission of applications to various Competent Authorities for specific approvals.

Several countries have also formulated biosafety regulations and guidelines on modern biotechnology for research, production processes, large-scale use of GMOs and products thereof and their release into the environment.

The website on Indian biosafety rules and regulations is to advise, facilitate and regulate modern biotechnology work at different stages to achieve the objectives of protecting the environment, including human and animal health, from the unintended adverse effects of GMOs and products thereof. This website was developed with the objective of facilitating and disseminating the statutory requirements to be adhered to by the researchers who are undertaking research work using modern biotechnology tools. As the knowledge in the area of modern biotechnology is ever expanding, biosafety guidelines can never be a one time exercise. DBT will continue to bring out the latest information and also modifications, amendments in the guidelines, *etc*., from time to time to the stakeholders through the website. All the relevant acts, rules, guidelines, proformas, stepwise procedures to be adopted for development of transgenic crops, r-DNA therapeutics, *etc*., to date can be viewed or downloaded from the website for compliance by the users of rDNA technology.

In addition to information exchange, the website provides tracking of regulatory clearance applications to Review Committee on Genetic Manipulation (RCGM) and e-monitoring of Institutional Biosafety Committees (IBSCs) on personalized web features.

Stacked Genes - *continued from page 2*

obligations beyond those required for each of the two individual trait parents if the gene stacking does not cause any metabolic changes. The Canadian Food Inspection Agency (CFIA) may be informed of stacked trait combinations obtained through traditional breeding techniques but would only evaluate stacked gene products if the data suggests that there may be an interaction between the stacked genes. CFIA reserves the right to request a review of the stacked plant if new issues arise regarding environment or livestock feed safety. The registrant is required to conduct an assessment for substantial equivalence and to notify the agency if any synergies or antagonisms or any potential problems are suspected as a result of the combination of genes.

In contrast, the European Union (EU), Argentina and Mexico require that bridging data for stacked traits be submitted as these products are considered new or unique by these regulatory authorities. The data includes composition, expression and a molecular fingerprint to verify the stability of the insert. The EU also requires a feeding study in chickens. Neither the EU nor Argentina has approved any stacked gene products to date but multiple product reviews are in progress.

VIEWPOINT:

Based on sound scientific principles and the extensive safety data generated to date on stacked gene products, it is recommended that:

1. Products resulting from transgenes combined by traditional methods that are not expected to exhibit any interactive effects, as in Categories 1 and 2, should be subjected to the same regulatory oversight that is routinely applied to products resulting from the combination of conventional traits via traditional breeding practices.
2. Products resulting from transgenes combined by traditional methods that are or may be expected to exhibit interactive effects as in Category 3, should be evaluated for such interactive effects. Food, feed and environmental safety data addressing the impact of such combinations on the metabolic and/or biosynthetic pathways affected would be submitted to the regulatory authorities.

In conclusion, based on scientific principles and significant experience with plant biotechnology products, there seems no justification for requiring products resulting from the combination of two unrelated or non-interacting traits that have been individually approved by the regulatory authority to undergo the full food, feed and environmental reviews required of the initial products.

GOVERNMENT ACCORDS APPROVAL TO THE NATIONAL BIOTECHNOLOGY DEVELOPMENT STRATEGY

PIB India - November 13, 2007

The National Biotechnology Development Strategy has been approved by the Government of India. The strategy is an outcome of a two-year-long nationwide consultation process with multiple stakeholders including concerned ministries, universities, research institutes, private sector, civil society, consumer groups, non-government and voluntary organizations and international bodies. The draft strategy, which was posted on the web, received over 300 comments from all sections of the society. The strategy has been finalized after careful scrutiny of these.

Announcing this at a press conference today the Union Minister for Science & Technology and Earth Sciences, Shri. Kapil Sibal said that recognizing that biotechnology is a sunrise sector thatrequires focused attention, the Government has accorded approval for the broad framework of this strategy and the sectors proposed therein. The strategy, while enabling the full utilization of currently available opportunities in manufacturing and services, will lay a strong foundation for discovery and innovation, effectively utilizing novel technology platforms with potential to contribute to long term benefits in agriculture, animal productivity, human health, environmental security and sustainable industrial growth.

See the full article at: http://www.agbios.com/sabp_main.php?action=ShowNewsItem&id=9005

INDIA OVERTAKES CHINA IN Bt COTTON RACE

Truth About Trade - November 9, 2007

Although China is an early starter in transgenic agriculture, India has overtaken its northern neighbour in terms of the area under Bt cotton cultivation and the number of genetically modified (GM) crops in the pipeline for approval.

Both the countries began with developing transgenic fibre crop - Bt cotton - and moved on to food crops. They are experiencing similar resistance from consumer groups and civil society organisations, which is considerably delaying the process of regulatory approvals. "We have developed transgenic rice, but the approval for commercial cultivation is withheld due to stiff resistance by Greenpeace. However, transgenic tomato, green pepper and petunia are in commercial cultivation in a few select areas," said Zhen Zhu of the Institute of Genetics and Development Biology in the Chinese Academy of Science, when recently in India.

See the full article at: http://www.agbios.com/sabp_main.php?action=ShowNewsItem&id=8994

We welcome reader comments or suggestions.
E-mail your letters to: nringma@agbios.com
Mail your letters to:
The Editor
SABP Newsletter
P.O. Box 475,
Merrickville, Ontario, K0G 1N0 Canada

SABP CONTACTS

South Asia

Dr. Vibha Ahuja
Deputy General Manager
Biotech Consortium India Limited
Anuvrat Bhawan, 5th Floor
210, Deendayal Upadhyaya Marg
New Delhi 110 002 India
Tel: 23219064-67
Email: vibhaahuja@biotech.co.in

Others

AGBIOS
106 St. John Street
P.O. Box 475
Merrickville, Ontario
K0G 1N0 Canada
Tel: +613-269-7966
Email: info@agbios.com

To receive an electronic copy of this newletter send your name and e-mail address to: info@agbios.com

USAID FROM THE AMERICAN PEOPLE
IFPRI
agbios