REPORT OF THE ROUND TABLE FOR BIOTECHNOLOGY IN COTTON

International
Cotton
Advisory
Committee

Discover
Natural
Fibres
Initiative

September 2013

REPORT OF THE ROUND TABLE FOR BIOTECHNOLOGY IN COTTON

Members

Dr. Keith Menchey	National Cotton Council, USA (Chairman)
Dr. Fernando Ardila	Instituto de Genética, CICVyA, INTA, Buenos Aires, Argentina
Mr. Adam Kay	Cotton Australia Ltd, Australia
Dr. Paulo A. Vianna Barroso	Embrapa, Goiás, Brazil
Mr. Eduardo Roman	Conalgodón, Colombia
Mrs. Luz Amparo Fonseca	Conalgodón, Colombia
Dr. Osama Ahmed Momtaz	Agricultural Genetic Engineering Institute, Egypt
Dr. Keshav R. Kranthi	Central Institute for Cotton Research, India
Dr. Tassawar Hussain Malik	Pakistan Central Cotton Committee, Pakistan
Mr. Hennie J. Bruwer	Cotton South Africa, South Africa

Library of Congress Cataloging-in-Publication Data

International Cotton Advisory Committee
Report of the Round Table for Biotechnology in Cotton
ISBN 9780963836199
Library of Congress Control Number: 2013915041

International Cotton Advisory Committee
1629 K Street, NW Suite 702
Washington, DC, 20006, USA
Telephone (202) 463-6660   Fax (202) 463-6950
Email address: <publications@icac.org>
http://www.icac.org/

Contents

Introduction

The International Cotton Advisory Committee decided at the 69th Plenary Meeting held in Lubbock, TX, USA in September 2010 to constitute a Round Table on Biotechnology in Cotton.' Although only 11 countries had commercialized biotech cotton at that time, it was decided that all member countries of the ICAC could participate in the Round Table. The objectives of the Round Table were to facilitate sharing of experiences on commercial production, marketing and regulation of biotech cotton. In January 2011, the ICAC Secretariat issued Memorandum No. 895 and invited member governments to nominate members for the Round Table. The Round Table was formed in April/May 2011, and Dr. Keith Menchey of the National Cotton Council of America volunteered to Chair the group.

The Round Table initiated discussions via email. The Chair asked members to give their views on the issues to be considered, and the members proposed the following:

1. Technical aspects that could have an impact on international trade.
2. Labeling of biotech products.
3. Growers are dependent on multinational companies that own technologies. The high cost of biotechnology (technology fee) is problematic.
4. Contamination of local materials with transgenic events is a concern.
5. Emphasis on breeding and genetic engineering for events related to climate and extreme conditions, such as drought, inundation and pests like boll weevil and whitefly, need emphasis.
6. Campaigns from green groups to convince governments to stop using biotech products are misleading.
7. High use of biotech products results in loss of biodiversity of native materials.
8. There is a need to educate the public.
9. Performance of biotech cotton in various countries across the globe and implications and impact of the technology on small growers including merits and challenges.
10. Country wise biosafety regulatory setup in place (and continuous update) to facilitate importation, testing, evaluation, approval and commercialization, and post release monitoring/issues of biotech cotton varieties.
11. Farmers are concerned about the disparity in the pricing of biotech seed among countries while the value of the technology is relatively consistent.
12. Barriers to technology transfer to developing countries and prospects for wider adoption of biotech cotton.
13. The Round Table should publish a white paper.

The Round Table met face-to-face two times in September 2011 at the 70th Plenary Meeting in Argentina and at the 71st Plenary Meeting in Interlaken, Switzerland. Summary reports from the meetings are attached as Annexes 1 and II.

Introduction

Lors de la 69ème Réunion plénière organisée à Lubbock, Texas, États-Unis, en septembre 2010, le Comité consultatif international du coton a décidé de constituer une Table ronde sur la biotechnologie et le coton. Même si le coton biotech n'était commercialisé que dans onze pays à ce moment-là, il a été convenu que tous les pays membres de l'ICAC pouvaient participer à la Table ronde. L'objectif de la Table ronde était de faciliter le partage d'expériences sur la production commerciale, la commercialisation et la réglementation du coton biotech. En janvier 2011, le Secrétariat de l'ICAC a publié le Mémorandum N°895 pour inviter les gouvernements membres à désigner les membres de la Table ronde. La Table ronde a été formée en avril/mai 2011. Le Dr. Keith Menchey du National Cotton Council of America s'est porté volontaire pour présider le groupe.

La Table ronde a engagé des discussions par courriel. Le Président a demandé aux membres de donner leur avis sur les sujets à examiner. Les membres ont proposé les thèmes suivants :

1. les aspects techniques susceptibles d'avoir un impact sur le négoce international ;
2. l'étiquetage des produits biotech ;
3. les cultivateurs dépendent des sociétés multinationales détenant les technologies. Le coût élevé de la biotechnologie (frais technologique) est problématique ;
4. la contamination du matériel local par des événements transgéniques suscite une inquiétude ;
5. il faudrait accorder de l'importance à la sélection et au génie génétique pour des événements liés au climat et aux conditions extrêmes, comme la sécheresse, les inondations et les ravageurs (par ex. le charançon de la capsule et la mouche blanche) ;
6. les campagnes des groupes écologistes pour convaincre les gouvernements d'arrêter d'utiliser les produits biotech sont trompeuses ;
7. l'utilisation importante des produits issus de la biotechnologie entraîne une perte de biodiversité au niveau du matériel indigène ;
8. il n'est pas nécessaire d'éduquer le public ;
9. les résultats obtenus avec le coton biotech dans différents pays du monde, ainsi que les implications et l'impact de la technologie sur les petits producteurs, notamment les avantages et les inconvénients.
10. la mise en place (et l'actualisation continue) d'un dispositif de réglementation de la biosécurité dans les pays afin de faciliter l'importation, les essais, l'évaluation, l'approbation, la commercialisation, ainsi que la surveillance et la prise en charge des problèmes après la commercialisation des variétés de coton biotech ;
11. les cultivateurs s'inquiètent de la disparité dans la détermination des prix des semences biotechs entre les pays, alors que la valeur de la technologie est relativement constante ;
12. les barrières au transfert de la biotechnologie dans les pays en développement et les perspectives pour l'adoption plus large du coton biotech. ;
13. la Table ronde devrait publier un livre blanc.

Les membres de la Table ronde se sont rencontrés à deux reprises, en septembre 2011 à l'occasion de la 70ème Réunion plénière en Argentine et en octobre 2012 lors la 71ème Réunion plénière à Interlaken, en Suisse. Des rapports de synthèse des réunions figurent dans les Annexes I et II.

Introducción

Durante su 69ª Reunión Plenaria celebrada en Lubbock, Texas (EE.UU.) en septiembre de 2010, el Comité Consultivo Internacional del Algodón decidió instituir una Mesa Redonda sobre Biotecnología en el Algodón. Aunque hasta entonces solamente 11 países habían comercializado el algodón biotec, se decidió que todos los países miembros del CCIA podían participar en la Mesa redonda. Los objetivos de la Mesa redonda eran facilitar el intercambio de experiencias sobre producción comercial, comercialización y reglamentación del algodón biotec. En enero de 2011, la Secretaría del CCIA emitió el Memorándum No. 895 invitando a los gobiernos miembros a designar a sus representantes a esta Mesa redonda que se constituyó en abril/mayo de 2011. El Dr. Keith Menchey del Consejo Nacional del Algodón de América, se ofreció como voluntario para presidir el grupo.

La Mesa redonda inició sus debates por medio de correos electrónicos. El Presidente pidió a los miembros sus opiniones acerca de los asuntos que debían considerarse, y los miembros a su vez hicieron las siguientes propuestas:

1. Aspectos técnicos que pudieran tener un impacto sobre el comercio internacional
2. Rotulado de los productos biotec
3. Dependencia de los productores de las compañías multinacionales propietarias de tecnologías. El alto costo de la biotecnología (la cuota tecnológica) presenta un problema
4. Preocupación por la contaminación de los materiales locales con eventos transgénicos
5. Énfasis sobre mejoramiento genético e ingeniería genética para lograr resistencia a fenómenos atmosféricos y condiciones extremas, como sequía, inundaciones y plagas (ejemplo, la plaga del picudo y la de la mosquita blanca) que requieren especial atención
6. Campañas engañosas utilizadas por grupos ecológicos con el fin de convencer a los gobiernos para que dejen de utilizar productos biotec
7. El alto uso de productos biotec que resulta en la pérdida de la biodiversidad de los materiales autóctonos
8. Necesidad de educar al público
9. Desempeño del algodón biotec en diversos países de todo el mundo, y las implicaciones y el impacto de la tecnología sobre los pequeños productores, incluidos tanto méritos como desafíos
10. Establecimiento (y constante actualización) del marco reglamentario de bioseguridad para cada país a fin de facilitar la importación, la aplicación de pruebas, la evaluación, la aprobación y la comercialización, así como la vigilancia posterior a la liberación y los asuntos relacionados con las variedades de algodón biotec
11. Preocupación entre los productores acerca de la disparidad entre los países al fijar los precios de las semillas biotec, mientras que el valor de la tecnología permanece casi constante
12. Barreras a la transferencia de tecnología a los países en desarrollo y perspectivas para una más amplia adopción del algodón biotec
13. Recomendación para que la Mesa redonda publique un documento blanco

Los miembros de la Mesa redonda se reunieron en persona dos veces en septiembre de 2011 durante la 70ª Reunión Plenaria en Argentina y en la 71ª Reunión Plenaria en Interlaken, Suiza. Se adjuntan sendos resúmenes de dichas reuniones como Anexos I y II.

Executive Summary

The adoption of biotech crops continues to spread to more countries. Fifteen countries -- Argentina, Australia, Brazil, Burkina Faso, China, Colombia, Costa Rica, India, Mexico, Myanmar, Pakistan, Paraguay, South Africa, Sudan and USA -- planted biotech cotton in 2012/13. Following South Africa and Burkina Faso, Sudan is the third African country to commercialize biotech cotton. Other countries in Africa have conducted trials and are close to commercializing biotech cotton.

From the 1960's to the 1990's, Australia relied almost exclusively on applications of insecticides, generally of limited modes of action. This limited range of chemistries inevitably led to pesticide resistance in key pests. Weeds were controlled through pre- and post-planting use of residual herbicides. Heavy reliance on chemical control by the cotton industry resulted in negative public perceptions, and Australia was in serious need of a technology that could reduce reliance on chemicals. Consequently, the Australian cotton industry moved to integrated pest management (IPM) techniques, and was one of the first adopters of biotech cotton in conjunction with IPM systems. Most varieties in Australia today contain the Bollgard II® and Roundup Ready Flex® traits together, and a smaller percentage of Liberty Link® cotton stacked with Bollgard II® is also planted. Australia implemented a strict biosafety regulatory system that has evolved over the years with risk to public health and environmental safety as its core principles. The regulatory system also strongly supports preemptive resistance management strategies

The success story of biotech cotton in various countries is similar – increased yields, reduced pesticide use, less tillage, increased worker safety - but critics continue to raise issues that cannot be proven scientifically. The crystal (Cry) toxins of Bacillus thuringiensis that were deployed in biotech cotton are safe for human consumption. The human stomach is acidic and contains proteases like pepsin, which degrade the Bt protein quickly. More importantly, the human intestine lacks the specific receptors to which the activated Bt proteins bind and initiate physiological effects.

Egypt has commercialized only biotech maize. However, biosafety regulations are in place in Egypt to commercialize biotech cotton and other crops. The Egyptian biosafety system includes legal authorities delegated to various agencies, assurances that the use of biotechnology products are safe, systematic reviews of biotechnology products, and a mechanism for public feedback. It is critical that an effective biosafety system includes mechanisms through which new information and accumulated experience can be incorporated into ongoing programs. It is important to encourage science-based decisions rather than politically motivated campaigns. Reinvesting in biotech research has an important bearing on moving biotech crops forward. Public awareness campaigns should explain economic and environmental benefits as well as the technical aspects throughout the chain of commerce including regulation, production, and trade.

The U.S. government decided against labeling food derived from biotech crops years ago as these products did not demonstrate safety concerns for humans or animals. The government has long held the policy that biotech food products are not "materially different" from conventional food products and, therefore, need no labeling. A number of surveys undertaken in the USA have shown that public opinion is in support of labeling biotech products if asked if they have a right to know about the food products that they buy. However, in other surveys with open-ended questions such as "what are your food safety concerns?" U.S. consumers consistently list biotechnology as a low priority. Opponents of labeling believe it would undermine both the labeling laws and consumer confidence. The European Union began requiring labeling for biotech foods in 1997 in response to consumers' concerns. Other countries including Russia, Japan, Australia, New Zealand, Turkey and China have also mandated labeling. In Australia, biotech foods and ingredients which contain novel DNA or protein that has come from an approved biotech food must be labeled with the words 'genetically modified'. However, foods that do not need to be labeled include highly refined foods, such as sugars and oils, where the process has removed DNA and protein from the food. In addition, labeling is not required where there is no more than 1% (per ingredient) of an approved biotech food unintentionally present in a non-biotech food. Labeling is not required in Canada.

Biosafety laws mainly focus, including the EU, on food and feed. Biotech cotton fiber is not included in Europe's biosafety regulations although cotton seed, meal, and oil are subject. While about one-third of world cotton fiber production is exported every year, only a small quantity of cotton by-products (seed, meal and oil) are exported. In terms of cotton fiber, Turkey's new Biosafety Law that became effective in September 2010, depending on its interpretation, could include fiber produced from biotech varieties. This law is probably the strictest among countries with biosafety regulations in place.

At the international level, Biosafety (Cartagena) Protocol, Codex Alimentarius, Food & Agriculture Organization of the United Nations, International Plant Protection Convention, Organization for Economic Cooperation & Development and World Health Organization have or claim a role in regulation of agricultural biotechnology and standard setting. Of these, the Cartagena or Biosafety Protocol (BSP) is most specifically focused on biotech crops and bears directly on the trade of biotech commodities. Adverse environmental impacts and risks to human health are the two most important clauses of the Cartagena or Biosafety Protocol.

Public perception of biotechnology is one of the critical issues in the further development, adoption, and free trade of biotech products. Public perception has resulted in a variety of regulatory restrictions among producing and consuming countries of biotech products. Anti-biotech groups have played a big role in stimulating public debate that is often times not based on science but on philosophical theories and fear. Apprehensions about the technology and stringent import restrictions in the EU are founded on the precautionary principle. In July 2010, the European Commission granted member states the authority to allow, restrict, or ban the cultivation of biotech crops on part or all of their territory. Consequently, a number of EU countries are planting biotech maize.

Given that importing countries have the right to ban any biotech product, technology developers play a crucial role in minimizing trade disruptions. Technology providers can make certain that legal approvals are completed in countries that are major and important markets for a biotech crop prior to commercialization. Governments can assist in this regard by diminishing the time between national and international approvals. With so many countries producing biotech crops and so many products and by-products coming out of biotech agricultural commodities, it seems unfeasible for importing countries to set a zero tolerance policy. Whatever the importing countries' policies are, they should be clear, and the industry must be aware of any such restrictions.

Experience with biotech cotton in Brazil, Colombia, Pakistan and South Africa has concluded that success of a biotech product could be hampered by local constrains and limitations. Although lepidopterans are very important in South and Central America, boll weevil is still the key pest in most of the countries in these regions, and the Cry insecticidal proteins present in biotech cotton do not affect the boll weevil or other sucking pests. The benefits of biotechnology in cotton observed in Africa, Asia, and the USA will only be achieved in Brazil and Colombia if boll weevil resistance is incorporated. The development of a boll weevil resistance trait is ongoing in public research institutes of Brazil and Argentina. In 2012/2013, Helicoverpa armigera that caused damage in some cotton regions was detected for the first time in Brazil. When this pest results in yield reduction and environmental costs due to higher use of insecticides, the area with biotech cotton will probably increase in Brazil. In Pakistan, the Cotton Leaf Curl Virus (CLCuV) has curtailed the adoption of biotech cotton. Resistance to the virus disease is a more serious problem than controlling lepidopterans. Farmers need CLCuV tolerant varieties, and only the eradication of this disease could ensure that farmers would benefit from the plant's inbuilt resistance to bollworms. In South Africa, low yielding cotton producers have not made use of biotechnology in cotton due to higher prices for competing crops.

All biotech cotton producing countries have reported some unintended consequences. The most common problem is the development of secondary pests. As pesticide applications for lepidopteran species declines, secondary pests, which had previously been inadvertently controlled by these applications, have increased in numbers to become primary pests. A resurgence of mirid bugs, and other minor pests, was reported in India and China. Colombia reported that the incidence and severity of diseases, particularly ramularia (Ramularia areola), anthracnose (Colletotrichum gossypii) and boll rot (disease complex), is higher in biotech cotton than in conventional cotton varieties. A rise in the incidence of diseases could be related to changes in the plant canopy and fruit allocation on the plant in a biotech cotton variety compared to a parental conventional variety.

Most of the reports provided to the Round Table on Biotechnology in Cotton from countries expressed concerns over the development of resistance by target pests. Resistance is likely if appropriate measures are not taken to delay and avoid resistance to a specific toxin. However, refuge requirements as a resistance management tool are being relaxed or ignored in some countries. It is imperative that pest populations be monitored for early detection of increased tolerance to the Bt toxin and to permit the implementation of mitigation measures early enough to prevent the actual development of resistance. In this regard, it is also important to monitor the level of toxin expression at various stages of growth and in different plant parts. Sub-standard expression of Bt toxin in biotech varieties only accelerates the resistance development process. In Pakistan, breeders and biotechnologists have been urged to improve the Bt toxin level of their varieties to an effective dosage level. Gene stacks for a particular trait, but of unrelated modes of action, provide an excellent option for resistance management, apart from enhancing the trait efficacy. However gene stacking can add to increased seed costs.

Private companies charge a fee for the technology in biotech cotton. Most countries reported concerns about the cost of biotech seed, which is considerably more expensive than that of non-biotech conventional planting seed. Farmers have often expressed their opposition to the high cost of technology in cotton and, in some countries, measures were taken to lower the cost of planting seed. The cost of biotech cotton seed has been prohibitive in rainfed production areas in South Africa where yields are lower. Technology fees for the same event may differ among different countries and even in different regions of the same country. However, according to the owners of the events, the value is proportional to the benefits provided to farmers.

Biotechnology applications in agriculture provide tools to modify plants precisely with desired traits. Cotton farmers around the globe anticipate commercial availability of a range of new biotech traits in the near future. It is important to develop biotech cottons to assist in the prevention of the distribution of phytosanitary problems such as Fusarium and Verticillium wilt as well as important regional pests and diseases, especially the boll weevil in Latin America and Cotton Leaf Curl Virus in Pakistan and

India. There is a need to strengthen the technology with additional genes through gene stacking to ensure long-term sustainability of various events. There are several sources other than Bacillus thuringiensis that have been used to isolate insecticidal genes. Genes from endo-symbiotic bacteria of nematodes, Xenorhabdus and Photorhabdus have been actively considered for the development of transgenic crops. Amongst animal sources, anti-chymotrypsin, anti-elastase, chitinase, cholesterol oxidase, and anti-trypsin have been isolated from the tobacco hornworm and used to develop biotech cotton resistant to sucking pests and lepidopteran insects. Trypsin inhibitors and spleen inhibitors isolated from cattle, protease inhibitors from plants (soybean, barley, cowpea, squash, mustard, rice, potato, tomato), amylase inhibitor genes from beans and cereals and lectins from plant sources have been used to develop biotech crops resistant to insect pests. Other gene sources include chitinases, glucanases, peroxidase, and tryptophan decarboxylase from various plant sources may also be useful transgenes to develop insect and disease resistant cotton. Replicase genes and coat protein genes have been used to develop leaf curl virus resistant varieties through over-expression of the proteins or silencing of the genes through RNAi, especially for countries in Africa, India, and Pakistan. The technology carries huge potential. It is not only inserting foreign or intra species genes, specific targets can also be achieved by gene silencing through RNA interference.

A lot of work is also going on to deal with abiotic stresses that the cotton plant faces in the field. Drought tolerant cotton is among many new avenues being extensively researched and some of the new traits are close to commercialization. Many drought related genes have been cloned and characterized in recent times. A number of potential genes have been shortlisted for fiber quality improvement, including a gene from spinach, a spider silk gene, and a gene from the silk worm. Good progress has already been made to develop ultra low gossypol cotton thus increasing the nutritional value of cotton seed. Molecular marker assisted breeding will of course bring precision and certainty to cotton breeding.

Résumé analytique

L'adoption des cultures biotechs continue de s'étendre à un plus grand nombre de pays. En 2012/13, quinze pays ont cultivé du coton biotech : l'Afrique du Sud, l'Argentine, l'Australie, le Brésil, le Burkina Faso, la Chine, la Colombie, le Costa Rica, les États-Unis, l'Inde, le Mexique, le Myanmar, le Pakistan, le Paraguay et le Soudan. Après l'Afrique du Sud et le Burkina Faso, le Soudan est le troisième pays du continent africain à commercialiser le coton biotech. D'autres pays africains ont réalisé des essais et sont sur le point de commercialiser le coton biotech.

Des années 1960 aux années 1990, l'Australie dépendait presque exclusivement des applications d'insecticides, aux modes d'action généralement limités. Le nombre limité de produits chimiques a inévitablement entraîné une résistance aux pesticides chez les principaux ravageurs. Les adventices étaient éliminées à l'aide d'herbicides résiduels avant et après les semis. La forte dépendance de l'industrie cotonnière envers la lutte chimique a donné lieu à des perceptions négatives auprès du public. L'Australie avait donc sérieusement besoin d'une technologie pouvant réduire cette dépendance envers les produits chimiques. Par conséquent, la filière cotonnière australienne s'est tournée vers les techniques de lutte intégrée contre les ravageurs (LIR). Elle a été l'un des premiers pays à adopter le coton biotech en combinaison avec les systèmes de LIR. À l'heure actuelle, la plupart des variétés en Australie contiennent les caractères Bollgard II® et Roundup Ready Flex®. Un pourcentage plus faible de coton Liberty Link® cumulant Bollgard II® est également cultivé. L'Australie a mis en place un système réglementaire strict sur la biosécurité qui a évolué au fil des années. Les risques pour la santé publique et la sécurité environnementale en sont les principes de base. Ce système réglementaire s'appuie également fortement sur les stratégies préventives de lutte contre la résistance.

Le succès du coton biotech est similaire dans les différents pays : amélioration des rendements, diminution de l'utilisation des pesticides, réduction du travail du sol et renforcement de la sécurité des travailleurs. Toutefois, les détracteurs continuent de soulever des questions qui ne peuvent être prouvées scientifiquement. Les toxines cristallines (Cry) de *Bacillus thuringiensis* présentes dans le coton biotech sont sans danger pour la consommation humaine. L'estomac humain est acide et contient des protéases comme la pepsine, qui dégradent rapidement la protéine Bt. Plus important encore, l'intestin humain est dépourvu des récepteurs spécifiques auxquels les protéines Bt activées se lient pour déclencher des effets physiologiques.

En Égypte, seul le maïs biotech a été commercialisé. Cependant, des réglementations sur la biosécurité sont en place dans le pays pour la commercialisation du coton biotech et d'autres cultures issues de la biotechnologie. Le système égyptien de biosécurité comprend des pouvoirs juridiques délégués à différents organismes, des garanties que les produits de la biotechnologie sont sans danger, des évaluations systématiques des produits biotechnologiques, ainsi qu'un mécanisme de rétroaction publique. Pour être efficace, il est essentiel qu'un système de biosécurité comprenne des mécanismes permettant d'intégrer les nouvelles informations et l'expérience accumulée dans les programmes en cours. Il est important d'encourager les décisions reposant sur une base scientifique, plutôt que les campagnes de motivation politique. Les réinvestissements dans la recherche biotechnologique ont une incidence considérable sur la progression des cultures biotechs. Les campagnes de sensibilisation du public devraient expliquer les avantages économiques et environnementaux, ainsi que les aspects techniques, dans l'ensemble du circuit commercial, notamment la réglementation, la production et le négoce.

Le gouvernement des Etats-Unis a décidé il y a plusieurs années de ne pas étiqueter les aliments dérivés des cultures biotechs car ces produits ne présentaient pas de risques pour les humains ou les animaux. Depuis longtemps, la politique du gouvernement est de considérer que les denrées alimentaires issues de la biotechnologie ne sont pas « matériellement différentes » des produits conventionnels et que, par conséquent, elles n'ont pas besoin d'être étiquetées. Plusieurs sondages réalisés aux États-Unis ont montré que l'opinion publique est en faveur de l'étiquetage des produits biotechs, quand on lui demande si le consommateur a le droit de connaître l'origine des denrées alimentaires qu'elle achète. Toutefois, dans d'autres sondages comportant des questions ouvertes (par ex. « quelles sont vos préoccupations en matière de santé ? »), les consommateurs américains attribuent systématiquement une priorité secondaire à la biotechnologie. Selon ses opposants, l'étiquetage nuirait aux lois en la matière et à la confiance des consommateurs. En réponse aux préoccupations des consommateurs, l'Union européenne a commencé à exiger l'étiquetage des aliments issus de la biotechnologie en 1997. D'autres pays, notamment la Russie, le Japon, l'Australie, la Nouvelle-Zélande, la Turquie et la Chine, ont également demandé l'étiquetage. En Australie, les denrées alimentaires ou les ingrédients biotechs contenant un nouvel ADN ou une nouvelle protéine provenant d'un aliment biotech approuvé doivent être étiquetés avec la mention « génétiquement modifiés ». Toutefois, les aliments hautement raffinés comme les sucres et les huiles, dont la transformation a éliminé l'ADN ou la protéine provenant de l'aliment, ne nécessitent pas d'étiquetage. Par ailleurs, l'étiquetage n'est pas requis lorsqu'il y a moins d'un pour cent (par ingrédient) d'un aliment biotech approuvé non intentionnellement présent dans une denrée alimentaire non biotech. L'étiquetage n'est pas exigé au Canada.

Les lois sur la biosécurité, notamment dans l'UE, portent principalement sur les aliments destinés aux humains et aux animaux. La fibre de coton biotech n'est pas incluse dans les réglementations européennes sur la biosécurité, bien que les graines, les tourteaux et l'huile de coton le soient. Environ un tiers de la production mondiale de fibre de coton est exportée chaque année, contre seulement une petite quantité de produits dérivés du coton (graines, tourteaux et huile). En ce qui concerne la fibre de coton, la nouvelle loi sur la biosécurité entrée en vigueur en Turquie en septembre 2010 pourrait, selon son interprétation, inclure la fibre produite à partir de variétés biotechs. Cette loi est probablement la plus stricte parmi les pays ayant mis en place des réglementations sur la biosécurité.

Sur le plan international, le Protocole de Carthagène sur la biosécurité, le Codex Alimentarius, l'Organisation des Nations unies pour l'alimentation et l'agriculture, la Convention internationale pour la protection des végétaux, l'Organisation de coopération et de développement économique et l'Organisation mondiale de la santé jouent ou revendiquent un rôle dans la réglementation de la biotechnologie agricole et l'établissement des normes. Le Protocole de Carthagène sur la biosécurité (PCB) porte plus spécifiquement sur les cultures biotechs et concerne directement le négoce des produits de base issus de la biotechnologie. Les impacts néfastes sur l'environnement et les risques pour la santé humaine sont les deux clauses les plus importantes du Protocole de Carthagène sur la biosécurité.

La perception de la biotechnologie par le public est l'un des enjeux essentiels dans l'avenir du développement, de l'adoption et du libre-échange des produits biotechs. Cette perception a entraîné un ensemble de restrictions réglementaires au sein des pays producteurs et consommateurs de produits issus de la biotechnologie. Des groupes opposés à la biotechnologie ont joué un rôle important en alimentant un débat public qui, souvent, n'a pas de fondement scientifique, mais repose sur des théories philosophiques et sur des craintes. Les appréhensions face à la technologie et les restrictions strictes sur les importations dans l'UE se basent sur le principe de précaution. En juillet 2010, la Commission européenne a conféré aux États membres le pouvoir d'autoriser, de limiter ou d'interdire la production des cultures biotechs sur une partie ou sur l'ensemble de leur territoire. Par conséquent, certains pays de l'UE cultivent du maïs biotech.

Étant donné que les pays importateurs ont le droit d'interdire tout produit biotech, les développeurs de technologie jouent un rôle crucial pour minimiser les perturbations des échanges. Les fournisseurs de technologie peuvent veiller à ce que les autorisations légales soient obtenues dans les pays représentant des marchés majeurs et importants pour une culture biotech avant la commercialisation. À cet égard, les gouvernements peuvent apporter leur contribution en réduisant le délai entre l'obtention des autorisations nationales et internationales. Compte tenu du nombre important de pays qui produisent des cultures biotechs et de produits et sous-produits dérivés des produits de base agricoles issus de la biotechnologie, il semble irréaliste que les pays importateurs établissent une politique de tolérance zéro. Quelles que soient les politiques des pays importateurs, elles devraient être claires, et la filière doit être consciente de telles restrictions.

L'expérience avec le coton biotech au Brésil, en Colombie, au Pakistan et en Afrique du Sud a montré que le succès d'un produit biotech pouvait être compromis par les contraintes et les limitations locales. Bien que les lépidoptères soient très présents en Amérique du Sud et en Amérique centrale, le charançon de la capsule reste le principal ravageur dans la plupart des pays de ces régions. De plus, les protéines insecticides Cry présentes dans le coton biotech ne sont pas efficaces contre le charançon de la capsule ou les autres insectes suceurs. Les avantages de la biotechnologie observés en Afrique, en Asie et aux États-Unis ne pourront être retirés au Brésil et en Colombie que si la résistance au charançon de la capsule est prise en compte. Le développement d'un caractère de résistance au charançon de la capsule est en cours dans les instituts publics de recherche du Brésil et de l'Argentine. *Helicoverpa armigera*, à l'origine de dégâts dans certaines régions cotonnières, a été détecté pour la première fois au Brésil en 2012/2013. La superficie consacrée au coton biotech augmentera probablement au Brésil lorsque ce ravageur entraînera des baisses de rendement et des coûts environnementaux en raison de l'utilisation accrue des insecticides. Au Pakistan, le virus de la frisolée du cotonnier (CLCuV) a limité l'adoption du coton biotech. Le problème de la résistance à cette virose est plus sérieux que la lutte contre les lépidoptères. Les cultivateurs ont besoin de variétés tolérantes au CLCuV et seule l'éradication de cette maladie pourrait garantir que les producteurs bénéficieraient de la résistance innée des cotonniers aux vers de la capsule. En Afrique du Sud, les producteurs de coton, qui enregistrent de bas rendements, n'ont pas adopté la biotechnologie en raison des prix plus élevés des cultures concurrentes.

Tous les pays produisant du coton biotech ont signalé des conséquences imprévues. Le problème le plus couramment rapporté concerne le développement des ravageurs secondaires. Étant donné la réduction des applications de pesticides pour lutter contre les lépidoptères, les ravageurs secondaires, qui étaient auparavant éliminés indirectement grâce à ces applications, se sont multipliés pour devenir des ravageurs importants. En Inde et en Chine, on a signalé la réapparition de punaises et d'autres insectes mineurs. En Colombie, l'incidence et la sévérité des maladies, particulièrement la ramulariose (*Ramularia areola*), l'anthracnose (*Colletotrichum gossypii*) et la pourriture des capsules (complexe de maladies), seraient plus importantes avec le coton biotech qu'avec des variétés conventionnelles. Une augmentation de l'incidence des maladies pourrait être liée à des changements au niveau du couvert végétal et de la répartition des fruits sur le cotonnier biotech par rapport à une variété conventionnelle parentale.

La plupart des rapports des pays fournis à la Table ronde sur la biotechnologie faisaient part d'inquiétudes sur le développement d'une résistance par les ravageurs ciblés. La résistance à une toxine spécifique est probable si des mesures appropriées ne sont pas prises pour la retarder et l'éviter. Toutefois, les exigences en matière de refuge, en tant qu'outil de gestion de la résistance, s'assouplissent ou ne sont pas respectées dans certains pays. Il est impératif de surveiller les populations de ravageurs pour détecter de manière précoce une tolérance accrue à la toxine Bt afin de pouvoir mettre en œuvre des mesures d'atténuation suffisamment tôt pour empêcher le développement effectif d'une résistance. À cet égard, il importe de contrôler le niveau d'expression de la toxine aux différents stades de croissance et à différents endroits sur les plantes. Une expression de la toxine Bt inférieure à la normale dans les variétés biotechs ne fait qu'accélérer le processus de développement de la résistance. Au Pakistan, on a exhorté les sélectionneurs et les biotechnologistes d'améliorer le niveau de la toxine Bt dans les variétés à un dosage efficace. L'empilement de gènes aux modes d'action différents pour obtenir un caractère particulier est une excellente option pour la gestion de la résistance, en dehors du renforcement de l'efficacité du caractère. Néanmoins, il peut alourdir les coûts des semences.

Les entreprises privées perçoivent des frais technologiques sur le coton biotech. La plupart des pays ont indiqué que le coût des semences biotechs est préoccupant, lesquelles sont nettement plus chères que les semences conventionnelles non biotechs. Les agriculteurs ont souvent exprimé leur opposition au coût élevé de la technologie pour le coton. Dans certains pays, des mesures ont été prises afin de réduire le coût des semences. Le coût des semences de coton biotech a été prohibitif dans les zones de production pluviale en Afrique du Sud où les rendements sont plus faibles. Pour le même événement, les frais technologiques peuvent varier selon les pays, voire entre les régions d'un pays. Toutefois, selon les détenteurs des événements, la valeur est proportionnelle aux avantages pour les cultivateurs.

Les applications biotechnologiques dans l'agriculture sont des moyens pour modifier les plantes de manière précise avec les caractères souhaités. Partout dans le monde, les producteurs de coton anticipent la disponibilité commerciale d'un éventail de nouveaux caractères biotechs dans un avenir proche. Il est important de créer des cotons biotechs contribuant à prévenir la propagation de problèmes phytosanitaires comme la fusariose et la verticilliose, ainsi que de ravageurs et de maladies importants à l'échelle régionale, surtout le charançon de la capsule en Amérique latine et le virus de la frisolée du cotonnier au Pakistan et en Inde. Il est nécessaire de renforcer la technologie avec des gènes supplémentaires grâce à l'empilement des gènes afin d'assurer la viabilité à long terme de différents événements. Plusieurs autres sources que *Bacillus thuringiensis* ont été utilisées pour isoler les gènes insecticides. Des gènes provenant de *Xenorhabdus* et de *Photorhabdus*, des bactéries endosymbiotiques de nématodes, ont été sérieusement étudiés pour le développement des cultures transgéniques. Parmi les sources animales, on a isolé et utilisé des inhibiteurs de la chymotrypsine, de l'élastase, de la chitinase, de la cholestérol oxidase et de trypsine pour la mise au point de coton biotech résistant aux insectes suceurs et aux lépidoptères. Des inhibiteurs de la trypsine et de la rate isolés de bovins, des inhibiteurs de protéases provenant de végétaux (soja, orge, niébé, courge, moutarde, riz, pomme de terre et tomate), des gènes inhibiteurs de l'amylase provenant de haricots et de céréales, ainsi que des lectines de sources végétales ont permis de créer des cultures biotechs résistantes aux insectes ravageurs. Des gènes d'origine végétale de *chitinase, glucanase, peroxydase* et *tryptophane decarboxylase* peuvent également être des transgènes utiles pour développer du coton résistant aux insectes et aux maladies. Des gènes de la réplicase et des gènes de protéine d'enveloppe ont servi à mettre au point des variétés résistantes au virus de la frisolée grâce à la surexpression des protéines ou le silençage génique par ARNi, notamment pour les pays africains, l'Inde et le Pakistan. La technologie comporte un potentiel énorme. Il ne s'agit pas seulement d'insérer des gènes étrangers ou intra-espèce, des objectifs spécifiques peuvent également être atteints par le silençage génique au moyen de l'interférence ARN.

De nombreux travaux sont également en cours pour traiter le problème des stress abiotiques auxquels le coton est confronté dans le champ. L'étude approfondie du coton tolérant à la sécheresse fait partie des nombreuses voies de recherches et certains nouveaux caractères sont sur le point d'être commercialisés. Récemment, les chercheurs ont cloné et caractérisé un grand nombre de gènes liés à la sécheresse. Plusieurs gènes potentiels ont été retenus pour l'amélioration de la qualité de la fibre, notamment un gène provenant des épinards, un gène de soie d'araignée et un gène du ver à soie. Des progrès satisfaisants ont d'ores et déjà été accomplis dans le développement du coton à très faible teneur en gossypol, augmentant ainsi la valeur nutritionnelle des graines des cotonniers. Bien entendu, la sélection assistée par marqueurs moléculaires apportera de la précision et de la certitude à l'amélioration variétale cotonnière.

Resumen Ejecutivo

La adopción de los cultivos biotec continúa expandiéndose a más países. Quince naciones -- Argentina, Australia, Brasil, Burkina Faso, China, Colombia, Costa Rica, Estados Unidos, India, México, Myanmar, Pakistán, Paraguay, Sudáfrica y Sudán – sembraron algodón biotec en 2012/13. Sudán, después de Sudáfrica y Burkina Faso, es el tercer país africano en comercializar algodón biotec. Otros países de Africa han llevado a cabo ensayos y están próximos a comercializar el algodón biotec.

Desde el decenio de 1960 hasta el decenio de los 90, Australia dependió casi exclusivamente de las aplicaciones de insecticidas como modos de acción generalmente limitados. Ese escaso arsenal de productos químicos inevitablemente llevó a que las principales plagas desarrollaran resistencia a los plaguicidas. Las malezas se controlaban mediante el uso de herbicidas residuales antes y después de la siembra. La fuerte dependencia de la industria algodonera del control ejercido a través de las sustancias químicas redundó en la formación de percepciones negativas entre la opinión pública, y Australia estaba muy necesitada de contar con una tecnología que le permitiera reducir su dependencia en esas sustancias. Por consiguiente, la industria algodonera australiana recurrió a las técnicas de manejo integrado de plagas (MIP) y fue una de las primeras en adoptar el algodón biotec conjuntamente con sistemas MIP. En la actualidad la mayoría de las variedades en Australia contienen las características Bollgard II® y Roundup Ready Flex® juntas, y también se siembra un porcentaje menor de algodón Liberty Link® apilado con Bollgard II®. Australia aplicó un estricto sistema de reglamentación de la bioseguridad que ha evolucionado con el transcurso de los años y que tiene como principios cardinales el interés por la salud pública y la inocuidad ambiental. Ese sistema de reglamentación también apoya denodadamente, las estrategias preventivas para el manejo de la resistencia.

El éxito del algodón biotec en diversos países es similar: aumento de los rendimientos, uso reducido de plaguicidas, menos laboreo, mayor seguridad en el trabajo – pero los críticos continúan planteando problemas que no pueden probarse con argumentos científicos. Las toxinas cristal (Cry) de *Bacillus thuringiensis* desplegadas en el algodón biotec son inocuas para el consumo humano. El estómago humano es ácido y contiene proteasas como la pepsina, que degrada rápidamente la proteína Bt. Lo que es más importante, el intestino humano carece de los receptores a los que se enlazan las proteínas Bt activadas y desatan efectos fisiológicos.

Egipto ha comercializado solamente maíz biotec. Sin embargo, en Egipto existen reglamentos de bioseguridad para comercializar el algodón biotec y otros cultivos. El sistema egipcio de bioseguridad incluye a autoridades jurídicas destacadas de diversas agencias, garantías del uso inocuo de los productos biotecnológicos, revisiones sistemáticas de los productos de la biotecnología y un mecanismo de retroalimentación abierto a la opinión pública. Es esencial que el sistema de bioseguridad incluya mecanismos para incorporar a los programas en curso las nuevas informaciones y experiencias acumuladas. Es importante estimular las decisiones basadas en fundamentos científicos y no las motivadas por campañas políticas. Las reinversiones en las investigaciones biotecnológicas contribuyen decisivamente al avance de los cultivos biotec. Las campañas de concienciación pública deben explicar los beneficios económicos y ambientales, así como los aspectos técnicos a lo largo de toda la cadena comercial, incluidos la reglamentación, la producción y el comercio.

Hace muchos años, el gobierno de Estados Unidos se opuso a que se rotularan los alimentos derivados de cultivos biotec dado que esos productos no representaban preocupaciones de seguridad alimentaria para seres humanos o animales. Desde hace mucho, el gobierno ha sustentado la política de que los productos alimentarios biotec no son "materialmente diferentes" de los convencionales y, por lo tanto, no requieren rotulado. Diversas encuestas realizadas en Estados Unidos han demostrado que la opinión pública apoya el rotulado si se pregunta a los consumidores si tienen derecho a saber acerca de los productos alimentarios que compran. Sin embargo, en otras encuestas con preguntas abiertas tales como "¿cuáles son sus preocupaciones sobre seguridad alimentaria?", los consumidores estadounidenses invariablemente dan a la biotecnología baja prioridad. Los que se oponen al rotulado consideran que las etiquetas socavarían las leyes de rotulado y la confianza del consumidor. La Unión Europea empezó a exigir rótulos en los alimentos biotec en 1997 como respuesta a las preocupaciones de los consumidores. Otros países, entre ellos Rusia, Japón, Australia, Nueva Zelanda, Turquía y China, también han impuesto el rotulado obligatorio. En Australia, los alimentos e ingredientes biotec que contienen ADN novel o proteínas provenientes de un alimento biotec aprobado deben llevar un rótulo con las palabras "genéticamente modificado". Sin embargo, entre los alimentos que no requieren etiquetas se cuentan alimentos altamente refinados, tales como azúcares y aceites de los que el procesamiento ha eliminado el ADN y la proteína. Además, no se exige etiqueta cuando un alimento biotec aprobado, que está casualmente presente en un alimento convencional, no sobrepasa el 1% (por ingrediente). Canadá no exige rotulado.

Las leyes de bioseguridad, incluso las de la UE, se centran sobre todo en alimentos para consumo humano y para consumo animal. La fibra de algodón biotec no está incluida en los reglamentos de bioseguridad en Europa, si bien la semilla, la harina y el aceite de algodón sí lo están. Aunque cerca de una tercera parte de la producción mundial de fibra de algodón se exporta anualmente, solo una pequeña cantidad de subproductos del algodón (semillas, harina y aceite) tiene como destino la exportación. En cuanto a la fibra de algodón (según la interpretación que se le dé a la Nueva Ley sobre Bioseguridad de Turquía), que entró en vigor en septiembre de 2010, dicha ley pudiera incluir fibras producidas a partir de variedades biotec. Esa legislación es probablemente la más estricta de todas las leyes sobre bioseguridad existentes en otros países.

A nivel internacional, el Protocolo de Cartagena sobre Bioseguridad, el Códex Alimentarius, la Organización de las Naciones Unidas para la Alimentación y la Agricultura, la Convención Internacional de Protección Fitosanitaria, la Organización para la Cooperación y el Desarrollo Económicos y la Organización Mundial de la Salud desempeñan o reclaman un papel en la reglamentación de la biotecnología agrícola y en la fijación de normas. De entre esos órganos, el Protocolo de Cartagena o de Bioseguridad (PCB) es el más centrado específicamente en los cultivos biotec y tiene que ver directamente con el comercio de productos básicos biotec. Dos de los artículos más importantes del Protocolo de Cartagena sobre Bioseguridad están relacionados con los impactos ambientales adversos y los riesgos a la salud humana.

El público percibe la biotecnología como uno de los problemas críticos para el ulterior desarrollo, adopción y libre comercio de productos biotec. La percepción pública ha generado una variedad de restricciones reglamentarias entre países productores y consumidores de productos biotec. Los grupos anti-biotec han desempeñado un fuerte papel en la estimulación del debate que con frecuencia no está basado en la ciencia sino en teorías filosóficas y en el temor. Las aprehensiones acerca de la tecnología y las estrictas restricciones a las importaciones en la UE se fundamentan en el principio precautorio. En julio de 2010, la Comisión Europea concedió a los estados miembros la potestad para permitir, restringir o prohibir los cultivos biotec en una parte o todo su territorio. Por consiguiente, diversos países de la Comisión Europea están sembrando maíz biotec.

Habida cuenta de que los países importadores tienen el derecho de prohibir cualquier producto biotec, los desarrolladores de la tecnología desempeñan un papel crucial en minimizar las disrupciones del comercio. Los proveedores de tecnología pueden garantizar que se completen las aprobaciones jurídicas en los mercados principales y de importancia para los cultivos biotec antes de su comercialización. Los gobiernos pueden asistir en ese sentido reduciendo el tiempo que media entre las aprobaciones nacionales y las internacionales. Con tantos países que producen cultivos biotec, y tantos productos y subproductos derivados de productos básicos biotec agrícolas, parecería imposible que los países importadores pudieran establecer una política de cero tolerancia. Cualesquiera que sean las políticas de los países importadores, esas políticas deben ser claras y la industria debe ser consciente de ese tipo de restricciones.

La experiencia con el algodón biotec en Brasil, Colombia, Pakistán y Sudáfrica permite concluir que el éxito de un producto biotec pudiera tropezar con restricciones y limitaciones locales. Es cierto que los lepidópteros son muy importantes en América Central y del Sur, pero el picudo sigue siendo la plaga fundamental en la mayoría de los países de esas regiones, y las proteínas insecticidas Cry presentes en el algodón biotec no afectan al picudo y a otras plagas de chupadores. Los beneficios de la biotecnología en el algodón observados en Africa, Asia y Estados Unidos se alcanzarían solamente en Brasil y Colombia si se incorpora la resistencia al picudo. El desarrollo del rasgo de resistencia al picudo no ha perdido vigencia en los institutos de investigaciones del sector público de Brasil y Argentina. En 2012/2013, *Helicoverpa armigera,* plaga que causó daños en algunas regiones algodoneras, fue detectada por primera vez en Brasil. Cuando esa plaga redunde en la reducción de los rendimientos y en costos ambientales debidos a un uso mayor de insecticidas, probablemente sea entonces cuando se extienda la superficie sembrada de algodón biotec en Brasil. En Pakistán, el virus de la rizadura de la hoja del algodonero (CLCuV) ha frenado la adopción de algodón biotec. La resistencia a la enfermedad del virus es un problema más serio que el control de los lepidópteros. Los productores necesitan variedades tolerantes al CLCuV y solo la erradicación de esa enfermedad pudiera garantizar que se beneficien los productores con la resistencia a los gusanos de la cápsula incorporada en la planta. En Sudáfrica, los productores de algodón de bajo rendimiento no han hecho uso de la biotecnología en el algodón debido a que se pagan precios más altos por los cultivos competidores.

Todos los países productores de algodón biotec han informado sobre algunas consecuencias no esperadas. El problema más común es el desarrollo de plagas secundarias. Con la reducción de las aplicaciones de plaguicidas contra las especies de lepidópteros, la densidad poblacional de las plagas secundarias, que antes se habían controlado colateralmente con esas aplicaciones, había crecido hasta convertirse en plagas primarias. El resurgimiento de los insectos míridos y de otras plagas menores se reportó en India y China. Colombia reportó que la incidencia y severidad de las enfermedades, en especial ramularia (*Ramularia areola*), antraknosa (*Colletotrichum gossypii*) y el complejo de la podredumbre de la cápsula (complejo de la enfermedad), son más elevados en el algodón biotec que en las variedades convencionales. La mayor incidencia de las enfermedades pudiera estar relacionada con cambios en el dosel de la planta y en la ubicación de la fruta sobre la planta en una variedad de algodón biotec en comparación con una variedad progenitora convencional.

Casi todos los informes de países presentados ante la Mesa Redonda sobre Biotecnología en el Algodón expresaron preocupaciones por el desarrollo de la resistencia en las plagas diana. Es probable que se desarrolle resistencia cuando no se adoptan las medidas apropiadas para retrasar y evitar la resistencia a una toxina específica. Sin embargo, los requisitos de refugio como instrumento de manejo de la resistencia se están relajando o pasando por alto en algunos países. Resulta imperioso vigilar las poblaciones de plagas para que se pueda detectar de forma temprana, una mayor tolerancia a la toxina Bt e implementar medidas de mitigación con suficiente antelación para prevenir el desarrollo cabal de la resistencia. En ese sentido, es importante también seguir de cerca el nivel de expresión de la toxina en diversas etapas de desarrollo y en diferentes partes de la planta. La expresión subestándar de la toxina Bt en variedades biotec hace acelerar el proceso de desarrollo de resistencia. En Pakistán, se ha instado a genetistas y biotecnólogos a que mejoren el nivel de toxina Bt de sus variedades llevándolo a un nivel efectivo de dosis. Los genes apilados para un rasgo en particular pero con modos de acción no relacionados, presentan una opción excelente para el manejo de la resistencia, aparte de elevar la eficacia del rasgo. Sin embargo, el apilamiento de genes puede encarecer más los costos de la semilla.

Las compañías privadas imponen una cuota por la tecnología en el algodón biotec. Los países en su mayoría comunicaron sobre preocupaciones acerca del costo de la semilla biotec, que es considerablemente más costosa que la semilla para la siembra convencional. Los productores a menudo han expresado su oposición al alto costo de la tecnología en el algodón, y en algunos países, se tomaron medidas para reducir el costo de la semilla para la siembra. El costo de la semilla de algodón biotec ha sido prohibitivo en las zonas de producción en Sudáfrica bajo condiciones de secano, donde los rendimientos son más bajos. Las cuotas tecnológicas para el mismo evento pueden diferir entre países e incluso entre regiones de un mismo país. No obstante lo ya dicho, según los propietarios de los eventos, el valor es proporcional a los beneficios que reportan a los productores.

Las aplicaciones de la biotecnología en la agricultura proporcionan el instrumental para modificar las plantas precisamente con los rasgos deseados. Los productores de algodón en todo el mundo están a la espera de la disponibilidad comercial de toda una serie de nuevos rasgos biotec en un futuro próximo. Es importante desarrollar algodón biotec que ayude a evitar la propagación de problemas fitosanitarios tales como la marchitez por *Fusarium* y por *Verticillium*, así como importantes plagas y enfermedades regionales, en especial el picudo en América Latina y el virus de la rizadura de la hoja del algodonero en Pakistán e India. Es necesario fortalecer la tecnología con genes adicionales mediante el apilamiento de genes que asegure la sostenibilidad a largo plazo de diversos eventos. Se han empleado otras fuentes ajenas al *Bacillus thuringiensis* que se han empleado para aislar genes insecticidas. Los genes de bacterias endo-simbióticas de nemátodos, *Xenorhabdus* y *Photorhabdus,* se han considerado insistentemente para el desarrollo de cultivos transgénicos. Entre las fuentes animales, anti-quimotripsina, anti-elastasa, quitinasa, colesterol oxidasa y anti-tripsina, se aislaron de la polilla manduca sexta y se emplearon en el desarrollo de algodón biotec resistente a las plagas de chupadores e insectos lepidópteros. Los inhibidores de tripsina y los inhibidores del bazo se aislaron en el Ganado; los inhibidores de la proteasa se aislaron en las plantas (frijol de soja, cebada, caupí, calabaza, mostaza, arroz, patata, tomate); genes inhibidores de la amilasa provenientes de granos y cereales, y lectinas de otras plantas se han utilizado para desarrollar cultivos biotec resistentes a las plagas de insectos. Otras fuentes de genes que incluyen *quitinasas, glucanasas, peroxidasas y triptofano decarboxilasa* provenientes de diversas plantas, también pueden resultar transgenes útiles para desarrollar algodón resistente a los insectos y a las enfermedades. Los genes de la replicasa y los de la proteína de la cápsula se han utilizado para desarrollar variedades resistentes al virus de la rizadura de la hoja mediante una sobreexpresión de las proteínas o el silenciamiento de los genes por medio de iARN, en especial para países de Africa, India y Pakistán. La tecnología encierra grandes posibilidades. No se trata solamente de insertar genes foráneos o intraespecíficos; también se pueden lograr metas específicas por medio del silenciamiento de genes a través de la interferencia de ARN.

Se está trabajando mucho también con miras a tratar el estrés abiótico que enfrenta el algodonero en el terreno. El algodón tolerante a la sequía está entre las muchas vías que se están investigando ampliamente y algunos de los nuevos rasgos están próximos a ser comercializados. Recientemente, se han clonado y caracterizado muchos genes relacionados con la sequía. Se han ido seleccionando y decanatando algunos genes con posibilidades para mejorar la calidad de la fibra, incluido un gen proveniente de la espinaca, uno de la tela de araña y otro del gusano de seda. Se ha alcanzado buen progreso en el desarrollo de algodón de gosipol ultra bajo, lo que aumentaría el valor nutricional de la semilla de algodón. La selección genética asistida por marcadores moleculares ciertamente aportará precisión y predecibilidad al mejoramiento genético del algodón.

Current Global Adoption of Biotech Crops

Keith Menchey, USA

Across the globe, more and more farmers are deciding to utilize biotechnology for higher yields and reduced production costs. Farmers have adopted crops genetically modified through modern biotechnology with the fastest adoption rate of any crop technology. First commercially available in 1996, the cultivation of biotech crops increased from 1.7 million hectares to 170 million hectares in 2012 - a 100-fold increase over the 17-year period. In 2011, there were 17.3 million farmers growing biotech crops in 28 countries around the world while biotech cotton is grown in 11 countries. The vast majority of these farmers (90%) were small, poor farmers from developing countries.

The rapid and vast adoption of biotech crops worldwide is a testament of the benefits these crops provide. These benefits have been documented in numerous articles (Brookes and Barfoot, 2011; Lusser *et al.* , 2012) and include decreased pesticide use, less energy inputs, and decreased tillage resulting in reduced soil erosion. Significant farmer benefits have come from biotech cotton. For example, over the 2002–09 period, the insect resistant *Bacillus thuringiensis* (Bt) cotton added US$7 billion worth of value to Indian farmers, cut insecticide use by half, helped to double yields, and turned the country from a cotton importer into a major exporter.

The United States continues to be the lead producer of biotech crops globally with 69.5 million hectares in 2012. The primary biotech crops grown in the U.S. are maize, cotton, and soybeans with an average adoption rate of around 90%. Other biotech crops are sugar beets, alfalfa, canola, papaya, and squash.

Following the U.S. in biotech crop production were Brazil (36.6 million hectares), Argentina (23.9 million hectares), Canada (11.6 million hectares), and India (10.8 million hectares). It is interesting to note that, of the 28 countries planting biotech crops in 2012, twenty were developing and eight were developed countries (Table 1). Developing countries grew 52% of global biotech crops in 2012 and, for the first time, exceeded the area planted in industrial countries in 2012. In 2012, the growth rate for biotech crops was twice as fast and twice as large in developing countries, at 11% or 8.7 million hectares versus 3% or 1.6 million hectares in industrial countries. It is estimated that for 2010 alone, the economic benefits from biotech cultivation in developing countries was US$7.7 billion.

Brazil is emerging as a global leader in biotech crops. For the fourth consecutive year in 2012 Brazil increased its biotech planting more than any other country in the world – a record 6.3 million hectares increase, resulting in an annual increase of 21%. Brazil has streamlined its regulatory system for new biotech events, which allowed faster approvals of new events. Brazil has also built the technical capability to develop its own events. The Brazilian Agricultural Research Corporation (EMBRAPA), a public sector research institution, has received approval to commercialize a biotech virus resistant bean variety developed entirely with its own initiative and resources.

In 2012, India marked its eleventh year of successful cultivation of biotech cotton during which the area planted to biotech cotton increased by a factor of over 200. Biotech cotton has had an incredible success story in India and has made cotton the most productive and profitable crop in the country. Biotech cotton has generated economic benefits for farmers valued at US$12.6 billion in the period 2002-11, reduced insecticide use by a half, contributed to the doubling of yields, and transformed India from a cotton importer to a major exporter. Pakistan approved biotech cotton in May 2010 and it is now the fourth largest biotech cotton growing country in the world. In 2012, biotech

Table 1. Global Area of Biotech Crops in 2012: by Country (Million hectares)**

Rank	Country	Area (Million Hectares)	Biotech Crops
1	USA*	69.5	Maize, soybean, cotton, canola, sugarbeet, Alfalfa, papaya, squash
2	Brazil*	36.6	Soybean, maize, cotton
3	Argentina*	23.9	Soybean, maize, cotton
4	Canada*	11.6	Canola, maize, soybean, sugarbeet
5	India*	10.8	Cotton
6	China*	4.0	Cotton, papaya, poplar, tomato, sweet pepper
7	Paraguay*	3.4	Soybean, maize, cotton
8	South Africa*	2.9	Maize, soybean, cotton
9	Pakistan*	2.8	Cotton
10	Uruguay*	1.4	Soybean, maize
11	Bolivia*	1.0	Soybean
12	Philippines*	0.8	Maize
13	Australia*	0.7	Cotton, canola
14	Burkina Faso*	0.3	Cotton
15	Myanmar*	0.3	Cotton
16	Mexico*	0.2	Cotton, soybean
17	Spain*	0.1	Maize
18	Chile*	<0.1	Maize, soybean, canola
19	Colombia	<0.1	Cotton
20	Honduras	<0.1	Maize
21	Sudan	<0.1	Cotton
22	Portugal	<0.1	Maize
23	Czech Republic	<0.1	Maize
24	Cuba	<0.1	Maize
25	Egypt	<0.1	Maize
26	Costa Rica	<0.1	Cotton, soybean
27	Romania	<0.1	Maize
28	Slovakia	<0.1	Maize

* 18 Mega countries growing 50,000 hectares, or more, of biotech crops
** Rounded off to the nearest hundred thousand

Source: Clive James, 2012

cotton was grown on nearly 10.8 million ha in India. The spread of biotech cotton contributed the achievement of a record production of 5.9 million tons in 2012/13.

Even in Europe where the resistance to agricultural biotechnology has been high, the number of hectares of the only biotech maize permitted to be cultivated increased from 114,490 hectares in 2011 to 129,071 hectares in 2012, an increase of 13%. In the EU, biotech crops were grown in five countries in 2012 - Spain, Portugal, the Czech Republic, Slovakia and Romania. Only two biotech crops are currently authorized for cultivation in the EU - insect resistant maize and a potato for industrial use.

Africa is steadily increasing the use of biotechnology. South Africa's biotech crop production was 2.9 million hectares 2012. Burkina Faso grew almost 300,000 hectares of biotech cotton in 2012 – more than double the 115,000 hectares grown in 2009. In 2012, Egypt continued to increase planting of biotech maize. An additional three countries - Kenya, Nigeria, and Uganda - conducted field trials, while Malawi has already approved ongoing trials. Kenya and Tanzania announced plans to start growing biotech cotton while Sudan commercialized biotech cotton in 2012 (Table 1 in previous page).

History and Impact of Biotech Cotton in Australia

Adam Kay, Australia

This section was adapted from an original article in the Farm Policy Journal. 8(1), 23-41 (2011).
Thanks to Dr. Sharon Downs (CSIRO Sustainable Ecosystems)
for updating references on Bt resistance

Greg Constable[1], Danny Llewellyn[2], Lewis Wilson[1] and Warwick Stiller[1]

Cotton has been cultivated in Australia since establishment of the first European settlement in 1788. However, the development of the Australian cotton industry really only began in the mid 1960’s when several local and American farmers saw the opportunity to grow irrigated cotton on the fertile black soil plains of northern New South Wales and southern Queensland. Since then, the industry has developed to a stage where cotton is Australia’s fourth largest rural export, with about 99% of cotton lint exported, generating export income in excess of $2 billion AUD in 2012. The cotton production system that has been developed is focused on achieving high yields of high quality fiber, ensuring Australian cotton is competitive in international markets and provides high returns per hectare and per mega liter of water.

Management of pests and diseases has been a key challenge to the industry since its inception. A range of key insect pests can reduce yield to virtually zero in some years if unmanaged.

From the 1960’s to 1990’s, pest management relied almost exclusively on regular application of insecticides, generally of a limited range of modes of action. This reliance inevitably led to selection for pesticide resistance in key pests, and associated problems of secondary pest outbreaks, induced by destruction of natural enemies of the pests.

Cotton is a poor competitor when young, and weeds can easily out-compete it. If weeds are poorly managed, they can dramatically reduce yield, harbor pests and diseases, and contaminate the lint at harvest. Reliance on residual herbicides applied before or at planting was the foundation for weed management for many years. However, this created another set of challenges due to the long residual activity and slow degradation of those herbicides. In combination, the previous heavy reliance on chemicals by the cotton industry resulted in negative public perception for the industry and posed a major threat to its ‘license to operate’.

By the mid 1990s, the Australian cotton industry was at a stage where it required a new wave of technology to transform the industry by reducing the need to apply pesticides. This section briefly outlines the history of the implementation of transgenic or genetically modified (biotech) cotton both for pest and weed management. The section also discusses regulatory requirements and issues, highlights the potential challenges associated with use of the technologies, reviews the benefits and shortcomings, and has a glance into the future.

Two broad types of biotech cotton have been commercialized in Australia. The first were pest resistant cottons containing one or more genes isolated from the soil bacterium, *Bacillus thuringiensis* var. kurstaki. These are commonly known as Bt cotton. The first biotech cotton released in Australia in 1996 contained the gene to produce the Cry1Ac protein, toxic to a range of Lepidopteran pests, including *Helicoverpa armigera* and *H. punctigera*, the primary cotton pests in Australia. This trait was known in Australia as Ingard®, and in the rest of the world as Bollgard®. A second Bt gene which produced the Cry2Ab protein with a different mode of action to Cry1Ac was subsequently added and cotton cultivars containing both these traits were made available commercially as Bollgard II® in 2003.

1) CSIRO Plant Industry, Locked Bag 59, Narrabri 2390, NSW.
2) CSIRO Plant Industry, PO Box 1600, Canberra 2601, ACT.)

The second form of biotech cotton to be released, available as Roundup Ready® in 2000, was resistant to the broad spectrum herbicide glyphosate, and allowed over the top application of glyphosate until plants reached four true leaves, after which some damage to developing pollen could impact yield. Greater flexibility of weed control was achieved in 2006 when Roundup Ready® was replaced with the improved Roundup Ready Flex® (RRFlex®) trait, which allowed over the top application of glyphosate throughout the entire growing season. Ingard, Bollgard II, and Roundup Ready traits are all from the Monsanto Company.

Liberty Link®, a herbicide tolerance trait from Bayer CropScience, which provides tolerance to the herbicide glufosinate, was made available to growers in 2007, but because of its narrower spectrum of weed control represents a relatively small part of the current production system. Although initially developed separately, it is now common for insect and weed resistant traits to be 'stacked' in the same cultivar. In 2011, more than 80% of biotech cotton cultivars sown in Australia contained the Bollgard II® and Roundup Ready Flex® traits together, and the small percentage of Liberty Link® cotton that was used was also mostly stacked with Bollgard II®.

Regulatory Oversight of Biotech Cotton

Regulatory frameworks for genetically modified species have been developed in most countries as biotechnology has advanced to the stage of practical application. In Australia, the Genetic Manipulation Advisory Committee (GMAC) was formed in 1987 to provide science-based risk assessment advice to government agencies, companies, and research organizations conducting genetic manipulation research and development. GMAC was responsible for the approvals of the initial laboratory and greenhouse work with Ingard® cotton from 1989 and, subsequently, the risk assessment and advice on its small-scale field testing from 1991 and then its later commercial release in 1996. Although cotton was one of the most frequently trialed biotech crops during the 1980's and 90's and the only one to be commercially released by 1996, GMAC was also involved in the assessment and approval of small scale planned releases of biotech canola, lupins, wheat, sugarcane, field peas, potatoes, tobacco, white clover and sub-clover, and carnations for the cut flower market.

By 2000, the regulatory framework within Australia had evolved into a new system with a dedicated authority backed by legislation. The Gene Technology Act 2000, which came into force on 21 June 2001, implemented a new national scheme for the regulation of biotech organisms that, while still being science-based like GMAC, also incorporated a specific legal framework to protect the health and safety of Australians and the Australian environment. The new Act conferred strong powers to Governments and regulators in the form of fines and prison terms to provide the public with high confidence that vested commercial interests would not circumvent the interests of the public or the environment. The powers of the Act were vested in a new Gene Technology Regulator (appointed by the Governor General and reporting to the Minister and Parliament) supported administratively by the Office of the Gene Technology Regulator (OGTR) and a number of expert and public committees to facilitate broad scientific and community input into decision making. The Regulator is responsible for identifying risks posed by or as a consequence of gene technology and managing those risks through a system of legally binding licenses, enforced by a monitoring and compliance unit within the OGTR. The processes have a high degree of public scrutiny, making the Australian system one of the most open and transparent biotechnology regulatory systems in the World (Timbs *et al.* , 2006; Dennis *et al.*, 2008).

During the period of transition from GMAC to the OGTR, an interim system was set up (the IOGTR) to formally ratify the commercial approvals for Roundup Ready® cotton that were then passing through GMAC. Since that time the OGTR has been responsible for subsequent assessments and approvals for the second-generation insect and herbicide tolerant cottons (Bollgard II®/Roundup Ready Flex®, and Liberty Link®), building on the previous research around safety and containment and commercial experiences with the first generation of biotech cottons.

Both GMAC and OGTR have coordinated with other federal and state bodies such as the National Registration Authority (now Australian Pesticides and Veterinary Medicines Authority - APVMA), Therapeutic Goods Administration (TGA), Food Standard Australia and New Zealand (FSANZ) the Federal and NSW and Queensland Environment Protection Authorities (EPA), and the NSW and Queensland state agricultural agencies. Although primarily an industrial fiber crop, cotton seed oil is used as human food and cotton fiber products are added to some consumer products such as toothpaste while cottonseed is fed to dairy cattle and other animals. Therefore, biotech cotton also requires approval as both food and livestock feed.

The issues of concern for regulators have remained largely the same for all the biotech cotton products released in Australia over the last 20 years. Containment of biotech traits to the trial site locations has clearly been an important issue for both the public and agencies like Environment Australia as it is critical to the ability to release and recall traits if unexpected social, health, or environmental outcomes become evident. It is particularly relevant through the period of small-scale field testing when a full regulatory safety assessment has not yet been carried out, but also during later commercial production when large areas are under cultivation. At an environmental level, any unintended impacts such as out-crossing of the traits to distantly related native species or deleterious effects on non-target organisms are clearly undesirable. They require assessment and/or supporting data to ensure that the risks of any potential environmental impact of using biotech traits are negligible. At an agricultural production level, poor efficacy, subsequent loss of efficacy through resistance development by the target organism(s), or disruption of existing management practices from volunteers also need to be evaluated and monitored during and after release. Each of these is discussed in more detail below.

Out-crossing and containment of biotech traits during early field testing

Cotton is essentially a self-pollinating species. Industry experiences with pure seed production, however, indicate that some out-crossing between cotton plants can occur in the field, mediated primarily by honey bees (*Apis mellifera*) and possibly some other insects. While the extent of out-crossing is relatively small it has required "off-types" to be removed during conventional seed production. This requirement indicated that some management would be necessary during the testing of "experimental" biotech traits to achieve high levels of containment. The known foraging behavior of bees means that the safest way to contain biotech traits and prevent transgenes escaping into adjacent unregulated crops is to embed them within fields of non-biotech cotton that would act as a buffer and serve as pollen "sinks". Australia has always adopted the "precautionary approach" to biotech regulation and all biotech testing has been staged up from small initial releases, building up to larger scales both at the experimental level and then during commercial release. During that process, data was routinely collected to measure the amount of gene flow away from the trial plots. These data established that there was little if any long-distance movement of pollen away from cotton fields and that a 20m buffer of non-biotech cotton surrounding field plots was sufficient to contain traits to the trial location (Llewellyn and Fitt, 1996; Llewellyn *et al.* , 2007). The use of physical isolation from other cotton or buffers is now considered standard practice for all new field trials of biotech cotton and other crop species in Australia.

While escape of transgenes into neighboring cotton crops is highly undesirable because of the commercial, social and agronomic production disruption it would entail, any potential wider environmental impacts of releasing biotech cotton also need to be managed. Cotton (*Gossypium hirsutum*) is an introduced species in Australia, which has a diverse flora of distantly related species (such as *Gossypium sturtianum* – Sturt's Desert Rose – the floral emblem of the Northern Territory). Escape of insect tolerance traits such as Ingard® or Bollgard II® into these native species could potentially enhance their rates of survival and turn them into environmental weeds. CSIRO was a center of expertise on the Australian native *Gossypium* species, both in their taxonomy and potential use for improvement of cultivated cotton [they are hardy, disease tolerant shrubs with a number of characteristics that have been lost from the cultivated species (Stewart, 1995)]. A considerable amount of research had already been carried out to move traits from the native species to cultivated cotton (mostly without success). While this suggested that natural gene flow in the other direction was unlikely, regulators required experimental validation. It was shown that hybrids were extremely difficult to produce through natural cross pollination and those few obtained were sterile. The native species rarely occur in land under agricultural production, often have flowering times that do not overlap with cotton and their genomes are highly incompatible. It was concluded that the risks of transgene flow from biotech cotton to the native species were negligible for any biotech trait (Brown *et al.*, 1997).

Non-target impacts of insecticidal traits

The potential effects of transgenic cotton on non-target species, especially arthropods (invertebrate animals having exoskeletons and segmented bodies: insects, spiders and crustaceans), have been the subject of considerable international research and sometimes controversy. During the mid-1990's, Australian scientists began the first field experimentation with biotech cotton expressing the Cry1Ac protein in Ingard®. The approach taken was to evaluate potential non-target effects directly in the field. This approach was considered more realistic than single or at most two or three species laboratory studies as it provided the opportunity to assess the potential non-target effects at the community level.

Initial studies showed no evidence of significant non-target effects in terms of abundance of species (Fitt *et al.*, 1994). In the following five years, a range of large scale (up to 10 ha) field experiments were completed which compared the abundance of arthropods in unsprayed conventional cotton, unsprayed biotech cotton, and conventional cotton that was sprayed for pests as dictated by standard industry practice at the time (Whitehouse *et al.*, 2005). In the first two of the four experiments conducted, only cotton expressing Cry1Ac was included but, in the subsequent two experiments, a predecessor of Bollgard II® which expressed Cry1Ac and Cry2Aa was also included.

Arthropod populations were sampled regularly through the growing season. Overall, the results showed that diversity was significantly reduced in sprayed conventional cotton compared with unsprayed conventional or biotech cotton. There were small but significant differences between unsprayed biotech cotton and conventional cotton that accounted for 4.5% of the variability. Across the 100 species groups examined, these differences were largely due to higher numbers of *Helicoverpa* in unsprayed conventional cotton as expected, as well as slightly higher numbers of Chloropidae (fruit flies), Drosophillidae, damsel bugs, and jassids.

These results suggest any non-target effects were small, especially when compared to cotton managed intensively with insecticides, and this has largely been borne out in the field since commercial release. Other studies in the USA, China and India have shown an essentially similar result (Marvier *et al.*, 2007; Naranjo *et al.*, 2005; 2008).

Volunteers and weediness potential of biotech cotton

The advent of glyphosate-tolerant cotton and especially the changeover from Roundup Ready® to Roundup Ready Flex® has provided great flexibility for cotton growers to manage weed populations. This enhanced control is especially true for some of the more recalcitrant weed species such as nutgrass (*Cyperus rotundus*) and for dryland growers where glyphosate facilitates zero tillage.

However, this crop resistance to glyphosate along with the general move to reduced tillage has led to increased survival of volunteer cotton plants on farms as a consequence of relying largely on glyphosate for most of the weed control. Volunteers originate from fallen seed cotton within fields, and along farm roadsides, channel banks and storages. Control of Bollgard II® volunteers in fields to be planted to conventional cotton, and vice versa, is a mandatory component of the Bollgard II® Resistance Management Plan (described below). They represent an unmanaged source of selection for resistance in *Helicoverpa* spp. and potentially other Lepidopteran species controlled by the Cry proteins expressed in the plants. However, volunteers elsewhere on the farm are not explicitly covered in the Resistance Management Plan.

Such volunteers represent a considerable risk to management of diseases, pests and of resistance to biotech crops in *Helicoverpa* spp. (see below) and biosecurity. Along with some weed hosts, they provide unmanaged hosts for a variety of pests and diseases. For instance, pests such as spider mites (*Tetranychus urticae*) and cotton aphids (Aphis gossypii) are frequently found in high abundance on the volunteers, and may migrate to nearby cotton crops and develop to damaging levels. Volunteers also often show symptoms of the aphid vectored disease Cotton Bunchy Top (see Reddall *et al.*, 2004 for information on this disease) and are an on-farm reservoir for the disease, which can be transmitted to crops by aphids. Similarly, such plants could be a problem if other exotic pests or diseases entered the country, especially the boll weevil (*Anthonomus grandis*) or 'viral diseases spread by aphids and other sucking pests.

Management of volunteers has been identified as a weak spot in use of transgenic cotton, and the industry has recognized the need to manage them more effectively. Recent outbreaks of the exotic mealybug, *Phenacoccus solenopsis*, which is extremely damaging and difficult to control, have been linked to the presence of higher densities of volunteers, within and around fields – providing another lever with which to encourage improved management. Recent extension efforts have strongly targeted control of volunteers as a key factor in reducing risks from pests and diseases and this is also a core practice emphasized in the industry's on-line Best Management Practice program, myBMP (www.mybmp.com.au).

The original approvals for Ingard® and Roundup Ready® in 1996 and 2000 respectively, restricted those biotech traits to south of latitude 22o S until studies could demonstrate the traits would not confer weediness in more tropical areas. Full approval was granted in 2006. Although volunteer cotton plants can also occasionally be found outside of cotton farms, studies in north-western Australia showed Ingard® cotton does not have the potential to be weedier than conventional cotton (Eastick and Hearnden, 2006). Monitoring of transport routes between gins in eastern Australia and dairies in more tropical Australia where cottonseed was used for animal feed did not indicate that there was a high risk of seed spilt during transport becoming roadside weeds (Farrell and Roberts, 2002). Further, a survey of the abundance of volunteers on roadsides revealed low densities with no particular bias toward higher establishment of transgenic plants (Addison *et al.*, 2007). The main factors limiting establishment and growth of cotton in these regions were frost, water, and grazing so the transgenic traits present in the plants offered no competitive advantage.

Food and feed safety of biotech cotton

All biotech traits go through a rigorous assessment for human and animal safety prior to approval by the OGTR for use in stock feed or by FSANZ for human food. As a result of international harmonization activities, the regulatory requirements are reasonably uniform across jurisdictions so one data set per trait is usually required and shared between agencies in different countries. The toxicological studies required involve the feeding of the purified novel proteins as well as the selectable marker that are expressed in the plants to a range of sentinel vertebrate and invertebrate animals to assess toxicity, potential allergenicity for the novel proteins, digestibility of the proteins, and an evaluation of the levels of nutrients or natural toxins in the biotech crop compared to that found in conventional cultivars.

Regulators use the concept of "substantial equivalence" between the biotech and non-biotech versions of the crop and the absence of acute toxicity of the introduced proteins to make decisions on the potential safety of the biotech plants. They do not require long-term animal or human feeding studies, but they do require considerably more than is required for the release of conventionally bred crops. In the case of Ingard®, Bollgard II®, Roundup Ready®, and RRFlex® cottons, this has involved the evaluation of the different insecticidal proteins Cry1Ac, Cry2Ab, the herbicide tolerance CP4 enolpyruvylshikimate-3-

phosphate synthase (EPSPS) proteins and the NptII antibiotic resistance protein and β–glucuronidase protein markers (present in Bollgard II®). Similar studies were required for the phosphinothricin acetyl transferase protein produced in Liberty Link® cotton. All of these proteins have been shown to have a safe history of use, low or no mammalian toxicity or allergenicity, and rapid digestion in the gut and so are considered to pose no risk to human or animal health. This safety finding has been borne out by the use of these same biotech traits in a variety of crops including corn, soybean, and canola for the last ten to fifteen years on over 160 million hectares worldwide in 2011 (James, 2012). Each new biotech trait released must go through the same assessment process, as the regulatory requirements have not changed significantly over time.

Biotech Cotton has Transformed Insect Management

The key pests of cotton in Australia are the larvae of two noctuid moth species, *Helicoverpa armigera* and *H. punctigera*. These larvae damage the growing terminals, sometimes causing excessive branching, and also destroy the developing flower buds (squares) and fruit (bolls) potentially reducing yield. *Helicoverpa* are present in large numbers in Australia (Fitt and Cotter, 2004) and unsprayed cotton can yield near zero as a result of their activity. Historically, management of these and other important pests such as cotton aphid, green mirid (*Creontiades dilutus*), and spider mites in Australian cotton has relied heavily on use of synthetic pesticides. This reliance has brought with it predictable problems of pesticide resistance, destruction of natural enemy populations resulting in pest resurgence and outbreaks of secondary pests (aphids, spider mites), human health concerns, and off-farm movement into sensitive riverine environments. These detriments have provided a strong impetus for the industry to reduce insecticide use.

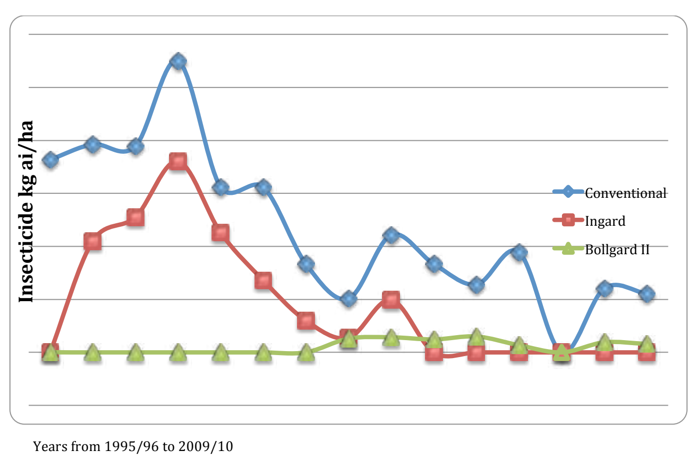
Pesticide resistance has been a major challenge, particularly in *H. armigera* that developed resistance to organochlorines in the early 1970's, endosulfan (cyclodiene) in the late 1970's, pyrethroids in the early 1980's (Forrester *et al.*, 1993), and carbamates in the mid 1990's (Gunning, Moores and Devonshire, 1996). Deployment of Ingard® cotton in the mid 1990's reduced insecticide use on those crops by about 50% (Figure 1), but efficacy was limited due to declining expression of Cry1Ac through the growing season. Ingard® cotton was always seen as an interim technology and, during this period, its production area was capped at 30% to reduce the risk that *Helicoverpa* spp. would develop resistance to this critical insecticidal protein. This restriction limited the influence of the technology on the industry. The strong reliance on insecticides continued on the remaining 70% of conventional cotton and led to ongoing selection for resistance to insecticides in *H. armigera*, secondary pest problems, and selection of pesticide resistance in these secondary pests. For instance, by the early 2000's spider mites were resistant to organophosphates (Herron *et al.*, 1998), the pyrethroid bifenthrin (Herron, Rophail and Wilson, 2001) and chlorfenapyr (Herron, Rophail and Wilson, 2004), and cotton aphids to organophosphates, the carbamate pirimicarb, and pyrethroids (Herron, Powis and Rophail, 2001).

The advent of more selective control options in the late 1990's (spinosad, indoxacarb and emamectin) offered the potential to manage *Helicoverpa* spp. more selectively. However, despite the cotton industry development of voluntary restrictions on the use of these compounds as part of an industry agreed Insecticide Resistance Management Strategy (e.g. Forrester *et al.*, 1993), their preferential use meant that, by the early 2000's, *H. armigera* showed incipient resistance to all three insecticides and pest management was on the verge of crisis.

The deployment of Bollgard II® in 2003/04, for improved resistance management and removal of the 30% area cap, resulted in a dramatic adoption of this technology. Currently, about 90% of the area is sown to Bollgard II cotton. It also led to a massive decline in pesticide use (by about 85%), especially relative to earlier years, but also in comparison with contemporary conventional cotton that had also significantly reduced its reliance on pesticides (Figure 1). Although expression of Cry1Ac tends to decline through the season, to the point that *Helicoverpa* larvae can survive, expression of Cry2Ab is higher and remains high enough to control *Helicoverpa* virtually all season allowing high levels of control to be achieved. This technology essentially saved the cotton industry from insecticide resistance problems with *H. armigera*.

A key benefit of the decline in use of insecticides was a co-incident decline in resistance frequencies in *H.*

Figure 1. Insecticide use on conventional, Ingard® and Bollgard II® biotech cotton in Australia for 15 years from 1995/96 to 2009/10. Data from Knox *et al.* (2004), updated with recent industry surveys.



armigera to the newer compounds, but also to most of the older compounds as well (Rossiter *et al.*, 2008). A range of other Lepidopteran species that previously also required control are also effectively controlled by Bollgard II®, including cotton tip borer (*Crocidosema plebejana*), cotton loopers (*Anomis flava)* and rough bollworm (*Earias huegeliana*). A few are still poorly controlled, including lesser armyworm (*Spodoptera exigua*) and in conventional area only, cluster caterpillar (*S. litura*). This control is a valuable benefit, especially for cotton tip borer that was previously controlled with broad-spectrum organophosphates that destroyed natural enemy populations and fostered outbreaks of spider mites.

The potential for *Helicoverpa* spp. to develop resistance to the Cry proteins was recognized long before the commercial release of Ingard®. Research developed a pre-emptive resistance management plan (RMP) designed to delay the development of resistance, especially in *H. armigera*, to ensure the technology lasted over the long term (Fitt, 2000). This species is more tied to cropping regions and diapauses in the soil of cotton crops through winter. These over-wintering pupae are the result of five or more generations of moths developed in the crop during the growing season all of which have all been heavily selected with pesticides and carry resistance potential to insecticides or Cry proteins from one season to the next (Fitt and Daly, 1990). Cultivation of the soil to a depth of 10 cm during late autumn to winter effectively reduced survival of these pupae and represents one component of a resistance management strategy. Despite being exposed to similar selection pressure from insecticides, the native *H. punctigera* has never developed resistance. This lack of resistance development is believed to be due to periodic and largely one-way migration of non-selected (susceptible) moths, from inland regions following suitable rains (Fitt, 1994). The theory is that these mate with those moths in cropping areas diluting any resistance. This phenomenon provided a model for developing a second strategy to limit development of resistance by *H. armigera* to insecticidal proteins in biotech cotton.

The RMP for Bt-cotton has four main elements: (i) cultivation of the soil in fields that were planted to insect resistant biotech cotton following harvest to destroy over-wintering pupae which may carry Bt resistance genes, (ii) growth of refuge crops to produce non-Bt selected moths to dilute resistance, (iii) use of defined planting windows to restrict the spread of sowing dates and, thereby, restrict the period of exposure of the technology across regions, and (iv) destruction of any volunteer plants.

These principles still form the core of the RMP and are a part of the technology license agreement signed by growers before they can purchase biotech cotton. Although the RMP has detractors due to the direct costs and opportunity costs involved, the high adoption of this technology shows that growers understand its critical importance and are willing to bear those costs to ensure that they have long term use of these technologies.

Resistance to both Cry1Ac and Cry2Ac in *Helicoverpa* spp. has been intensively monitored since the first registration of Ingard®. This research has assumed even greater significance and effort since the deployment of Bollgard II® and the relaxation of the cap on the area that can be grown to biotech cotton (Downes *et al.*, 2007). Genes conferring some resistance to Cry1Ac or Cry2Ab have been identified from individuals of *H. armigera* and *H. punctigera* collected from the field. Background levels of resistance to Cry2Ab, in both *Helicoverpa* species are significantly higher than were expected and assumed in the models used to evaluate the effectiveness of the RMP in delaying resistance from causing field failures in insect control. For *H. armigera*, there has not been a statistically significant increase in resistance to Cry2Ab (Mahon *et al.*, 2007; Downes and Mahon, 2012a) during the period of monitoring. In *H. punctigera*, the frequencies of Cry2Ab resistance genes has been steadily increasing since Bollgard II® was adopted up to 2009/10 (Downes *et al.*, 2010; Downes and Mahon, 2012b). The industry's Transgenic and Insecticide Management Strategies (TIMS) Committee reviews the outcomes of insecticide and Bt resistance monitoring annually and, in conjunction with the Monsanto Company, will update the RMP as required. For example, the Monsanto Company is developing a contingency plan to mitigate the risk from any further increases in resistance, although there have not yet been any field failures to control these pests. Additionally, Monsanto's Bollgard III trait (Bollgard II plus Syngenta's VIP gene, an insecticidal protein with a different mode of action again than either Cry1Ac or Cry2Ab) is being developed to further add insurance against resistance to individual genes. Research on resistance to Vip3A has begun and early results suggest that while background levels of resistance in both *Helicoverpa* species are significantly higher than expected, Vip3A resistant individuals are susceptible to Cry1Ac and Cry2Ab (Mahon *et al.*, 2012).

Bollgard II® cotton is highly resistant to *Helicoverpa* spp. infestation (Lu *et al.*, 2012a). Nevertheless, Bollgard II® crops are regularly checked for the presence of surviving larvae and, in some fields, *Helicoverpa* spp. larvae have survived to the third or fourth instar. Whitburn and Downes (2009) reported that from 2005-08, on average 15% of the area planted to Bollgard II® in any season carries *Helicoverpa* spp. larvae at levels that exceed recommended thresholds (2 larvae > 3mm long/m2 of cotton in two consecutive checks or 1 larva > 8mm long/m^2). These larvae are not physiologically resistant to Bt and, despite, these occasional events, the overall performance of Bollgard II® has been good as reflected by the ongoing low pesticide usage in such crops. In fact the insecticide use on Bollgard II® cotton has decreased even further as growers gain more confidence in applying damage thresholds for all pests before resorting to using sprayed insecticides (Figure 1). Furthermore, Bollgard II cotton compensates well for damage caused by larvae and the current threshold can be used in most situations without causing significant yield reduction (Lu *et al.*, 2012a, b).

As expected, the decline in pesticide use on Bollgard II® cotton has allowed other pests to survive. These secondary pests include a range of sucking pests that would formerly have been coincidentally controlled by insecticides applied against *Helicoverpa* species. The most significant among these is the green mirid, which feeds on developing squares and bolls causing younger bolls to shed and damaging the lint in maturing bolls - potentially reducing yield. A lack of validated thresholds or sampling strategies in the mid 2000's created uncertainty in the industry about management of this pest. Coupled with higher cost of more selective control options and low cotton prices, mirids were often sprayed with cheap broad-spectrum products leading to outbreaks of mites or aphids in some cases. Since then, there has been development and validation of improved sampling protocols and thresholds. In conjunction with increasing evidence that control at below threshold levels has no benefit (Whitehouse, 2010), this data led to more rational mirid management.

Over the past 10 years, B-Biotype *Bemisia tabaci* (silver leaf whitefly – SLW) has gradually become a pest across the Australian cotton industry. This pest excretes sticky honeydew that contaminates cotton lint and reduces its value (Gunning *et al.*, 1995; De Barro *et al.*, 2011). It was first reported in cotton regions in 1994 (Gunning *et al.*, 1995) and the first major outbreak occurred in the northern production region in 2001/02. The reasons for the gradual rise in pest status of this species are complex but, essentially, it gradually displaced a non-pest native *Bemisia tabaci* biotype already in Australia (De Barro *et al.*, 2011) and outbreaks have now been reported from virtually all regions. Fortunately, there are well established sampling protocols, threshold, and control options for effective, albeit expensive, management of this pest (Sequeira and Naranjo, 2008). Local research has shown no difference between conventional cotton and Bollgard II® in attractiveness for SLW, but okra leaf cultivars tend to harbor about half as many SLW (Wilson, unpub. data). However, the SLW problem has not yet caused growers to plant okra leaf varieties and the bulk of cotton grown is normal leaf shape.

A range of other minor pests have occurred over the past 10 years, some related to Bollgard II® and some not. Reduced spraying has allowed survival of pale cotton stainers (*Dysdercus sidae*), jassids (Austroasca viridigrisea) and thrips (*Frankliniella schultze*i and *F. occidentalis*) late in the season and in some years these species have all caused damage and sporadically required control. The latter are also valuable predators of mites (Wilson *et al.*, 1996) and provide significant suppression of mite populations especially in Bollgard II® crops.

Despite some of the challenges mentioned above, the advent of Bollgard II® has been a spectacular success in reducing pesticide use against *Helicoverpa* species and has had the spin-off of substantially increased beneficial populations in these crops which have helped to manage other pests (Mansfield *et al.*, 2006) and resulted in a significant improvement over Ingard® (Figure 1).

Weed Management in Herbicide Tolerant Cottons

In Australia, weeds are generally less of a problem in cotton than insects but many areas do have a reasonably high incidence of problematic weeds (Werth *et al.*, 2006) particularly on former grazing and/or flood prone land. Weed control systems have changed in the last decade from a mechanical cultivation-based system with residual herbicides and hand hoeing to a system of minimal cultivation with the use of herbicide tolerant cultivars and few if any residual herbicides (Charles and Taylor, 2003).

Cotton cultivars containing the Roundup Ready® trait were sown commercially for the first time in Australia in the 2000 planting season. These cultivars contained the EPSPS gene from the CP4 strain of *Agrobacterium* that provides tolerance to the herbicide glyphosate (Barry *et al.*, 1997). The gene expresses an enzyme which is highly tolerant to growth inhibition by glyphosate and, hence, plant metabolism is not disrupted by the herbicide. Glyphosate could only be applied over the top of these cultivars at early growth stages (up to 4 leaves) because, although the plants had excellent vegetative tolerance to the herbicide, reproductive tolerance was minimal and glyphosate reduced pollen development. The original Roundup Ready® trait was phased out in 2006 and replaced with Roundup Ready Flex®, incorporating a second CP4 EPSPS gene expressed highly in floral tissue. This stack gives Roundup Ready Flex® cotton cultivars season-long tolerance to glyphosate (May *et al.*, 2004).

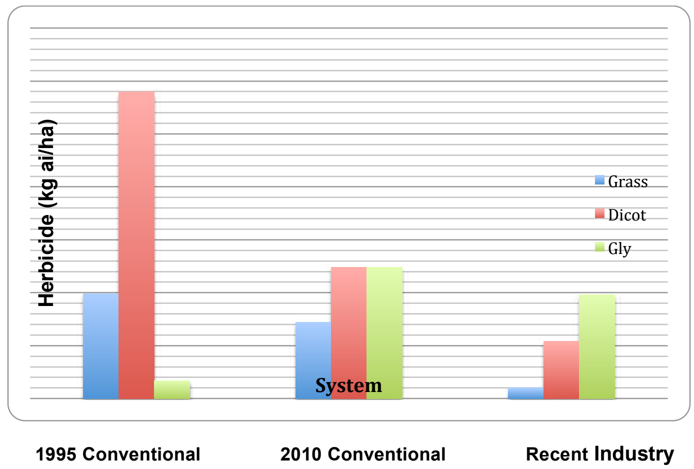
Cultivars containing an alternative herbicide resistance trait from Bayer CropScience, called Liberty Link®, became available in 2007. This trait expresses the phosphinothricin acetyl transferase gene (pat) from a Streptomyces bacterium that provides tolerance to the herbicide glufosinate (Leemans *et al.*, 1992). This herbicide has a different mode of action to glyphosate and, although it also has a broad spectrum of activity, it has relatively lower efficacy on grass weed species.

In the 2011 planting season, over 98% of the crop contained the Roundup Ready Flex® trait. Over-reliance on glyphosate as the primary weed management tool in a farming system is of concern and has major implications for weed management including species shift in the weed spectrum and development of herbicide resistant weeds. These potentials highlight the necessity for continuing to adopt an integrated approach to weed management. The license for use of Roundup Ready Flex® and Liberty Link® cottons contains RMP conditions to inspect for weed survivors after application of glyphosate or glufosinate. If weeds are present, they must be removed by other methods.

A detailed survey of herbicide use and practices was conducted in 2009/10 to identify amounts of herbicide applied to herbicide tolerant crops. This survey indicated that total herbicide application to non-herbicide tolerant cotton averaged 3.90 kg a.i. per ha. In contrast, herbicide tolerant cotton such as Roundup Ready Flex® and Liberty Link® averaged 2.02 kg a. i. per ha - 52% of that applied to non-herbicide tolerant crops. This reduction was predominantly due to farmers no longer using residual herbicides in many fields of herbicide tolerant cotton (Figure 2) and, in some instances, with only glyphosate being used.

Kennedy *et al.*, (2011) have shown that a Roundup Ready® weed management system can pose a lower risk to the environment than conventional weed management systems because less residual herbicides are used. The high use of glyphosate in conventional weed systems in 2010 reflects the increasing use of glyphosate in fallow preceding the cotton crop. The earlier survey by Werth *et al.*, (2006) showed higher use of glyphosate at that time (some applied as shielded sprays in crop) compared with 2010.

Figure 2. Herbicide use on conventional and Roundup Ready Flex® cotton in Australia. Data from Charles *et al.*, (1995) for conventional cotton (1995con); 2010 conventional (2010con) and 2010 Roundup Ready Flex® (2010RR); data from recent industry survey. Residual Grass herbicides were Trifluralin, Pendimethalin and Metolachlor; Residual Dicot herbicides were Fluometuron, Prometryn and Diuron; and Gly is glyphosate



Integrated weed management (IWM) is based on the philosophy of using a range of weed management methods in combination, so that all weeds are controlled by at least one component of the weed management system. Thus other management options for weed control such as inter-row cultivation and crop rotation are also still practiced. Weed management options are available on line (www.cottoncrc.org.au/industry/Publications/Weeds/WEEDpak).

Crop Agronomy in Biotech Cotton

Conventional cotton grown in Australia traditionally had herbicide and insect damage. The advent of biotechnology has led to crops with more normal architecture for the first time. The genes being expressed for resistance to insects or herbicides do not directly have any impact on plant growth, development, or yield. However, those traits can have an indirect effect on plant growth and may affect crop management.

Figure 3. An example of plant morphology change than can occur with insect damage to a conventional cotton plant (left) compared with a Bollgard II® plant (right). Damage to the growing point resulting in vegetative regrowth and loss of fruit is evident in the conventional plant.

In the case of resistance to an herbicide such as glyphosate, there can be reductions in the phytotoxicity of residual herbicides that are replaced by a glyphosate system. Figure 2 shows the reduction in residual herbicides in a Roundup Ready Flex® herbicide program. Also, with reduced need to incorporate these residual herbicides, there can be reduced tillage allowing seedlings to be more vigorous in an herbicide tolerant system compared with a conventional system that relies on incorporated residuals.

In insect resistant cotton, where better control of *Helicoverpa* spp. larvae is achieved, there can be a substantial change in plant morphology as a result of reduced damage to the main stem and less loss of fruit (Figure 3). These changes will reduce plant height and promote earlier crop maturity. The consequences will be earlier demand for nutrients so that fertilizer application strategies (timing, form, and rate) may vary between biotech and conventional cotton. Earlier maturing crops may also require different irrigation strategies. Yeates *et al.*, (2010) found that, where better *Helicoverpa* control was achieved with Bollgard II®

cotton, the Bollgard II crop was more susceptible to water stress during the late boll fill period than conventional cotton and when irrigated with optimum scheduling, was more water-use efficient (yield per unit of water use) than conventional cotton. Where there was no difference between Bollgard II and conventional cotton in pest control, there was no difference in irrigation requirement or water use efficiency. Earlier harvest facilitates earlier soil preparation and/or better timing of transition to a following rotation crop such as wheat.

Another consequence of potential earliness from better *Helicoverpa* control in Bollgard II® is more flexible sowing dates. Bange *et al.*, (2008) found that Bollgard II could be sown later than conventional cotton and still achieve maximum yield because the more rapid crop setting allowed a later sowing to set and mature a full crop. An additional benefit of later sowing was more favorable fiber quality parameters such as fiber length and micronaire that could add value to the harvested crop. Delayed sowing can also reduce the incidence of seedling disease and other diseases such as Fusarium Wilt that are favored under cooler conditions.

Other agronomic factors such as optimum plant density have no difference between transgenic and conventional cotton systems (Brodrick *et al.*, 2010).

Breeding Challenges with Biotech Cotton

Gene introduction (transformation) in crop plants requires a tissue culture phase to regenerate whole biotech plants. Efficiency and success through this process in cotton varies quite significantly between different cultivars making it difficult to introduce genes directly into specific elite cultivars. Parallel introduction of traits directly into different cultivars would in any case add significantly to registration costs as each different transgenic event would need to be registered, not just each biotech trait. As a result, most introductions of commercial traits in cotton have been done with the highly transformable cultivar Coker 312 (May *et al.*, 2003) although this cultivar has not been grown commercially for some time. Once transformation with a trait of interest has been achieved, an elite event identified, and preliminary field testing has been successful, the trait then needs to be registered and subsequently incorporated by breeding into elite cultivars suited to the cropping systems of the regions in which it is to be cultivated. Australia has its own unique cultivars to address the specifics of our soil, climate, disease, and market requirements in addition to high yield potential (Constable *et al.*, 2001).

A new trait is generally backcrossed to the best currently available commercial cultivars. Backcrossing is a relatively simple process where a recurrent parent (adapted, productive cultivar) is crossed to a donor parent (un adapted, but carrying the biotech trait of interest). Beginning in the F1 generation, the hybrid material is successively backcrossed several times to the recurrent parent. After each backcross, selection is made for the biotech trait. A sufficient number of backcrosses must be made to recover all the desirable traits of the recurrent parent while retaining the additional biotech trait. Between three to five backcrosses have been used in CSIRO's cotton breeding program. In practice however, the process of recovering all desirable traits is not easy. Stiller *et al.*, (2006) evaluated the effect of three, four and five backcrosses on yield, quality, and disease resistance parameters of cotton. It was concluded that it was not necessary to have any more than three backcrosses for most of the major agronomic traits in the resulting populations. However, it was clear from the greater than expected diversity of lines derived from backcrossing that the breeder should place more emphasis on subsequent selection and testing using appropriate population sizes to adequately recover (or even improve on) the desirable traits of the recurrent parent. In fact, it has been very clear from cultivar adoption rates that growers will not adopt inferior cultivars regardless of the presence of biotech traits. As backcrossing takes a few years breeders need to pre-emptively utilize elite germplasm from their breeding programs to try and anticipate the suitability of that trait in different germplasm lines currently under development (Verhalen *et al.*, 2003).

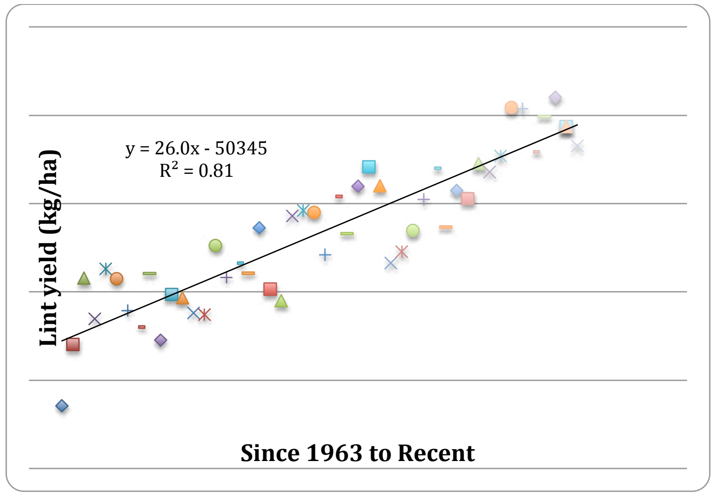
The change in plant architecture associated with better *Helicoverpa* control and high fruit retention also has consequences for the ideal plant type/growth habit of cotton cultivars that might be developed. Conventional cultivars with earlier crop maturity and more compact growth habit, as required in shorter growing seasons to the south and eastern regions in Australia, were found to be unsuitable for incorporating of Bt transgenic traits such as Ingard® and, especially, Bollgard II®. This unsuitability was due in most instances to the high fruit retention, which resulted in smaller plants to such an extent that the number of fruiting branches and yield potential was reduced. As a consequence, the suite of successful commercial cultivars in the Bollgard II® era since 2004 has drifted towards longer season types which maintain yield potential.

The development of the first transgenic trait in cotton and its introgression to modern Australian cultivars coincided with the appearance of a new strain of Fusarium Wilt in Australia (Kochman, 1995) and soon after by a need to change fiber quality characteristics to better suit the requirements of modern cotton spinning mills in the export market (May and Taylor, 1998). The multigenic nature of resistance to diseases such as Fusarium Wilt (Constable *et al.*, 2007), Verticillium Wilt (Bolek *et al.*, 2005) and Bacterial Blight (Hillocks, 1992; Bird, 1982) as well as fiber quality (May, 1999; Lacape *et al.*, 2005; Park *et al.*, 2005) requires careful breeding in terms of crossing and backcrossing strategies and large population sizes in early generation breeding. The end result can be slower development and delivery of transgenic cultivars with the danger of delaying the appearance of new higher yielding genotypes with transgenic traits.

Other future transgenic needs include enhanced insect and weed resistance options as well as water and nitrogen use efficiency. Tools for breeding such as marker assisted selection will also play a more important role in screening for many conventional and transgenic traits and enhance new cultivar development and commercialization.

The improved insecticide and herbicide practices resulting from the deployment of Bollgard II® and Roundup Ready Flex® cotton have been highlighted in Figures 1 and 2 which show 80% reductions in the use of insecticides and a 50% reduction in the use of residual herbicides per hectare by farmers growing cultivars with biotech traits. These changes in agricultural pesticide practice as well as changes in pesticide registrations have resulted in substantial reductions in pesticides found in river systems in cotton growing areas (Mawhinney, 2011).

Figure 4. Progress with lint yield of the Australian cotton industry since 1963.



High adoption of biotech traits in Australian cotton reflects the innovation and vision of growers to constantly improve and address new challenges. The industry continues to improve in yield by 26 kg lint/ha/year (Figure 4) and the biotech era since 1996 has at least maintained if not increased that improvement. Yield increases have come from both breeding and crop management; it is important to note that biotech cotton has not been introduced for higher yield potential; rather, the technology is used to reduce reliance on pesticides.

The biotech cotton experience has been a striking success in Australian agriculture. The high adoption rate of the current technology shows that industry regards it as a good value for pest and weed management. Transgenic traits such as Bollgard II® and Roundup Ready Flex® have led to significant reductions in the amount of insecticides and residual herbicides applied to cotton. Observed trends in industry pesticide use also indicate growers are becoming more familiar and confident with the performance of these traits in the management of their crops. Yields are also continuing to rise. The overall farming system is becoming more efficient as well as more environmentally friendly. Resistance Management Plans are understood and adopted by cotton growers, despite their additional costs or inconvenience. The weed RMP in Australia, for example, appears to have been more effective than that used in the US where resistance to glyphosate has already occurred (Powles, 2008).

Aside from the considerable impact of biotech cotton on insect and weed management, it is worthwhile to reflect that some of the side-benefits have also played a huge role in the high rates of adoption. Greater ease of pest management has led to an improved lifestyle – with less need for spray equipment, reduced stress and urgency with pesticide requirements before *Helicoverpa* larvae or weeds are too large to control. Further, less time taken managing *Helicoverpa* has provided crop managers with greater opportunity to focus more on improved agronomic management which has been crucial during the last decade with prolonged drought and low prices.

Biosafety Regulations, Safety and Public Education

Osama A. Momtaz, Egypt, and Keshav Kranthi, India

The progress in research and development of biotech cotton is currently being debated with biosafety issues in perspective. While supporters of biotech cotton, technology developers and many scientists have been reporting the benefits of the technology, many anti-biotechnology activists have been trying to highlight negative reports of biotech crops on animal health and environment. The success story of biotech cotton in India and many other countries has been subjected to debate. Though it has been amply clear that the reports of 'Goat, sheep and cattle death due to grazing in biotech cotton fields in India' were not based on any scientific evidence, the activist campaign created doubts and mistrust in the minds of general public.

The Bt Cry toxins deployed in biotech cotton have been considered safe for human beings. The stomach of humans is acidic and contains proteases like pepsin, which degrade the Bt protein. More importantly the human intestine lack the specific receptors to which the activated Bt protein binds and initiates the physiological effect that occurs in Lepidopterans.

A recent report (Seralini *et al.* 2012) linked Roundup Ready biotech maize with development of cancers in Sprague Dawley rats. The paper raised serious concerns and had potential implications to create political opposition to the approval of herbicide resistant biotech cotton in several countries, including India. However, within a week of its publication, there was strong criticism from a large section of the scientific community (EFSA, 2012), followed by condemnations and rejection of the methodology, statistical analysis, results and conclusions.

While biotech food crops and biotech cotton for insect resistance through multiple gene stacking and resistance to herbicides have been under cultivation in many countries, their entry into new areas is being debated for prospective benefits and biosafety issues. However, many countries have examined the biotech cotton products from a scientific perspective and have permitted area-wide usage to harness the benefits.

According to the United Nations' World Population Prospects, for the last 50 years, world population has multiplied more rapidly than ever before. In 1950, the world had 2.5 billion people. By 2005, the world had 6.5 billion people. By 2050, global population could rise to more than 9 billion. Most of this growth will occur in the less developed countries in Africa, Asia, and Latin America whose population growth rates are much higher than those in more developed countries. Scientists and policy makers are asking how the food, feed, and fiber needs of such a population can be met. Compounding this challenge, climatic changes may potentially reduce world agricultural productivity and increase agricultural prices worldwide,

Africa's increasing desire to utilize science and technology to enhance agricultural productivity to meet the nutritional needs for its growing populations has become a mandatory national quest. After years of political neglect, the challenge of feeding increasing national populations has forced policy makers to restructure their strategy of relying upon food and feed imports to a more active policy of utilizing new technologies in the agricultural sector to focus on cultivating and using national resources to meet these challenges. Policy makers and agricultural specialists are focusing on agricultural biotechnology and have initiated the formation of regulatory and technical structures for developing, planting, trading, and promoting biotechnology applications to confront these challenges.

The development and adoption of biotech cotton has been shown to hold potential for increasing cotton production, decreasing environmental impacts, reducing pesticide use, and enhancing natural resource diversity. While recognizing the potential of agricultural biotechnology to enhance sustainability and productivity in the agricultural sector, the government of Egypt is also aware of some public concerns about the potential risks of agricultural biotechnology to food safety, the environment, and genetic resources.

Egypt ratified the Cartagena Protocol in 2003 and has made remarkable progress in designing and implementing a national biosafety system using existing international guidelines and involving international experts. The Agricultural Genetic Engineering Institute, Egypt has been a focal point for introducing agricultural biotechnology in Egypt, the Middle East and North Africa region, and Africa through the development of a flexible biosafety system for biotech products. As this regulatory system matures, insight is gained as to its strengths and weaknesses.

Regulatory Framework for Biosafety in Egypt

Following obligations under Article 8g of the Convention on Biological Diversity (CBD), Egypt was among the first countries to establish regulations for biosafety in 1995. Since 1995, these regulations have been regularly updated and refined, taking into account new developments such as the coming into force of the Cartagena Protocol on Biosafety. Over the years, the national regulatory framework for biosafety in Egypt has evolved.

In Egypt, the Ministry of Agriculture (MOA), in coordination with the Ministry of Environment (MOE) and other stakeholders, has been the major authority in drafting the biosafety bill for the regulation of commercialized biotech crops and their products.

The Egyptian biosafety system is based on four elements:

- **Legal Authorities**

  Documents implementing biosafety policy include new regulations, adaptation of existing regulations, or non-legislative guidelines issued such as by Ministerial Decree. Such documents typically authorize the formation of national and institutional biosafety review committees, specify their respective duties and membership, and describe application and review procedures for environmental releases of biotech crops.

- **People**

  Applicants seeking to conduct field tests of genetically modified organisms and members of review committees should be equal and collaborative partners in ensuring the safe use of biotechnology products. Both need to be familiar with the environmental risk/benefit issues associated with biotechnology products and have a working knowledge of the biosafety review process.

- **The Review Process**

  Biosafety review is a systematic evaluation of the specific biotech crop, the site where it will be released, and the conditions under which the release will be conducted. If a potential risk is identified, appropriate management procedures are built into the release plan to reduce the risk to an acceptable level.

- **Mechanisms for Feedback**

  Agricultural biotechnology remains a field in which risk/benefit assessments and risk management decisions are hindered by knowledge gaps and a lack of data. Thus, it is critical that an effective biosafety system includes mechanisms through which new information and accumulated experience can be incorporated. Technical information and scientific data gathered from previously approved releases could be used to support subsequent biosafety reviews. Field test information and assessments from other countries may also be useful as long as potentially significant differences in the environment, affected ecosystems, and agronomic practices are recognized.

Public Awareness and Acceptance

In the very earliest stages of Egypt's biotechnology research program, leading proponents recognized that public acceptance was essential for successful integration of biotechnology into the Egyptian agricultural system. Accordingly, different methods were applied to provide the public with accurate information through various venues including newspaper articles, workshops, TV programs, and the Internet. More efforts are needed in this field because any negative anti-genetically modified organisms activist article that appears in newspapers, magazines, and on TV, will cause inflammatory messages and magnifying the more radical political arguments seen and heard in Europe, India, and elsewhere. The lack of understanding in the media confused the public; many people came to believe that biotechnology products are tainted with conspiracy plots and corruption. Public educational activities must be continual as messages from anti-biotech activists can lead to confusion or suspicion in the public and the media.

Encouraging science-based decisions rather than politically based decisions has been an important component of moving biotech crops forward. The timing and strength of this anti-biotech media campaign in Europe apparently caught the biotechnology community completely unprepared. Months passed before biotechnology proponents began to mount a public response.

The following objectives are offered for consideration to address current challenges for marketing biotech cotton in Africa.

1- Maintain public awareness campaigns throughout the different levels of the market chain including farmers, consumers, and policy makers, explaining the economic and environmental benefits as well as the technical aspects dealing with the process of regulation, cultivation, and trade.

2- Develop plans for national biosafety needs and set policy frameworks at national and regional levels for strengthening and encouraging the process of planting and trading genetically modified organisms using biotechnology.

3- Cooperation and co-integration with international organizations to promote biosafety regulation and risk assessments as well as risk management and mitigation for biotech cotton in Africa.

Technology Costs

Most countries reported that there is a concern about the cost of biotech cotton seed, which is considerably higher than that of traditional cotton seeds. In Pakistan, these costs continue to rise and may preclude the small farmers, which comprise the majority of the cotton growing community of Pakistan, from continued use of the technology. Farmers are concerned that, in the years to come, even larger farmers may not be able to purchase high cost biotech cotton seeds.

Brazil reports that the technology fee is not the same for all events. The same event may have different value in different countries and even in different regions of the same country and, according to the owners of the events, the value is proportional to the benefits brought to the farmers. In Brazil, the price of the Bollgard I cotton event that has been available for some years has been considered excessive, particularly when noting the less intricate pest complex in Brazil compared to other countries and the production problems with some of the transgenic cultivars. The combination of high technology fees and poor agronomic performance of the varieties resulted in relatively low adoption rates in Brazil until 2011.

Farmers in South Africa have a high concern over the price they have to pay for biotech seed and technology fee which is substantially more expensive than conventional seed. The pricing system applied over the years has had a depressing effect on the planting of biotech cotton in rainfed production areas in South Africa. Some cotton farmers in these areas believe that the yield increases and savings on insecticide chemicals are not large enough to offset the additional technology fee for seed.

As in other markets, the issue of pricing for the technology in South Africa is one that merits consideration in a broader sense.

The cost of seeds is one of several inputs in an overall production system whose output must offset the production cost to ensure profitability. In South Africa, farmers planted other crops when the world cotton prices were very low. In the last two years since cotton prices have increased, some farmers have shifted back to cotton production but now lack access to harvesting equipment which places profitability of this production in question.

Because agricultural production and markets are continuously changing, there has been a growing dialogue between seed companies and farmers who access their products. In markets such as South Africa, this dialogue has sometimes resulted in adjustments in the technology fees to meet customer's needs and sometimes resulted in greater offerings of conventional seed.

South African farmers have benefited from the introduction of biotech cotton. However, the job creation, rural development, and economic growth potentials of biotech cotton have been limited as the technology was introduced into a struggling sector that were faced with lower world cotton prices, cheap textile and garment imports, and higher comparative prices for competing crops like maize, soybeans, and sunflower seed. Though the technology increased productivity, it has not yet made South Africa competitive in the world market.

(The South African part was ccompiled by Cotton SA from collective data received from cotton farmers in South Africa)

Labeling and Technical Aspects with Potential Impact on International Trade

Fernando Ardila, Argentina

The U.S. federal government determined years ago that products derived through biotechnology have not been scientifically demonstrated to be harmful to human or animal health and, therefore, do not require labeling. In addition, it has also determined that biotech food products are not "materially different" from conventional food products and, therefore, need no label.

In 1992, the U.S. Food and Drug Administration (FDA) ruled against requiring labels for foods derived from biotech crops. In its labeling policy statement, the FDA says, "The agency is not aware of any information showing that foods derived by these new methods differ from other foods in any meaningful or uniform way, or that, as a class, foods developed by the new techniques present any different or greater safety concern than foods developed by traditional plant breeding."

Public opinion polls, however, find that Americans want to know what is in their food and heavily favor the labeling of food products that contain genetically modified ingredients. In March 2011, an MSNBC Health poll revealed that support for biotech labeling stood at nearly 90 percent. According to one pollster, "A free market depends on open information from which to base decisions." These types of polls, in most cases, do not include questions that address the costs of such labels. The International Food Information Council has been doing consumer surveys for years and consistently find that, given an open-ended questions on their concerns about food safety, biotechnology has always appeared near the bottom of the list. Consumers seem to be much more concerned about issues such as microbial contamination and pesticide residues.

In recent years, citizens' initiatives on biotech labeling have gained support. The Committee for the Right to Know, a grassroots coalition of consumer, public health, and environmental organizations, has collected enough citizen signatures to qualify its initiative on the California ballot for the November election. Its bill, the California Right to Know Genetically Engineered Food Act, would require all foods containing ingredients derived from biotech crops to be labeled. There have been similar state bills introduced over the years, all being defeated, but the population of California makes this initiative particularly important. The biotechnology industry, agricultural interests, and food processors are opposed to mandatory labeling, saying it will only bewilder a public that is not well informed about genetic engineering and that extra labeling would only confuse the consumer since it differentiates products that are not really different, making it harder for consumers to make logical choices. In addition, it is stated that requiring labeling for ingredients that do not pose a health issue would undermine both the labeling laws and consumer confidence. Ensuring that such labeling is accurate would also put a huge burden on regulatory agencies. Because of such concerns from industry and fearing a lack of sales, it is nearly impossible to find biotech foods in the European Union and Japan both of which have laws that require labeling. The European Union began requiring labeling for biotech foods in 1997 "in order to respond to consumers' concerns and enable them to make an informed choice; and to avoid misleading consumers." Other countries around the world have followed its lead in mandating labeling, including Russia, Japan, Australia, New Zealand, and China. Like the U.S., no labeling law exists in Canada despite numerous surveys indicating up to 90 per cent of Canadians want mandatory labeling of biotech food. Canada's leading national consumer group does not support mandatory labeling. Instead, the Consumers' Association of Canada supports voluntary labeling, backing the stance of the Canadian Food Inspection Agency .

In Australia, biotech foods, ingredients, additives, or processing aids which contain novel DNA or protein that has come from an approved biotech food must be labeled with the words 'genetically modified'. Labeling is also required when genetic modification has resulted in an altered characteristic in the food, such as a change in the nutritional components in the food compared with the conventional form in the case of high oleic acid soybeans. Labeling is not for safety reasons, as only those biotech foods assessed as safe are approved for sale. There are some exemptions to the Australian food labeling requirements. Foods that do not need to be labeled as genetically modified include highly refined foods, such as sugars and oils, where the process has removed DNA and protein from the food , including novel DNA and novel protein. In addition, labeling is not required where there is no more than 1% (per ingredient) of an approved biotech food unintentionally present in a non-biotech food.

The World Health Organization has stated that “GMO foods currently available on the international market have passed risk assessments and are not likely to present risks for human health,” “In addition, no effects on human health have been shown as a result of the consumption of such foods by the general population in the countries where they have been approved.”

The Codex General Standard for the Labeling of Prepackaged Foods Codex Stan 1-1985 (Rev. 1-1991) includes relevant information for the consumer. It allows labeling when exclusively informing any differences about composition, nutritional value, and proposed use with respect to the homologous conventional food. This statement gives no support to the criteria that find the necessity of labeling foods that, without any change in composition, nutritional value and proposed use, are composed with or derive from genetically modified organisms using biotechnology. Since such information is absent from the label of conventional food, there is no reason for that kind of discrimination related to production method.

In this sense, it is interesting to refer to the decision of the WTO Dispute Settlement Body through the dispute settlements Dispute Ds135 European Communities — Measures Affecting Asbestos and Products Containing Asbestos and Dispute DS231 European Communities — Trade Description of Sardines. In these cases, it was established that there are three critical requirements for a regulation being considered as a technical rule: 1) that characteristics can be established from it, 2) that these characteristics can be applied to identified products, and that 3) they are of a mandatory nature. Then, technical rules may establish characteristics of products and their production methods. However, they could only establish conditions over production methods when they are related to the final product. These criteria mean that if, by any reason, the characteristics of any production method are not reflected in the final product, these characteristics must not be the target of any regulation or constraint for the product to be sold let alone in the frame of any technical rule of a mandatory nature for all the parties.

The characteristics of the product should then be verifiable over the product itself and any label should include information that may be verifiable in the final product.

Trade Implications and Other Issues of Concern

Keith Menchey, USA

Trade Situation

World cotton fiber trade is largely defined by its two dominant countries - China for imports and the United States for exports with each country accounting for about 40% of world trade (Figure 5).

Cotton seed is normally consumed domestically or exported within a limited basis. The weight to volume ratio for cotton seed is low making it cost prohibitive for long distance transport. For example, U.S. cotton production occurs in the 17 southern states and cotton seed is exported almost exclusively to Mexico. The major exporters of cotton seed are the U.S. and Australia. The major importers include China, Japan, South Korea, and Mexico (Figure 6).

Cottonseed meal or cake is used for feed for adult ruminants and organic fertilizers. Cotton seed contains gossypol, which is highly toxic to monogastrics and even sometimes to calves. The major exporter of cake is the U.S. followed by China, Benin, and Zimbabwe. The major importers are Mexico, Iran, and South Africa (Figure 7).

Cottonseed oil has many food applications including

Figure 5: Cotton Fiber Exports/Imports

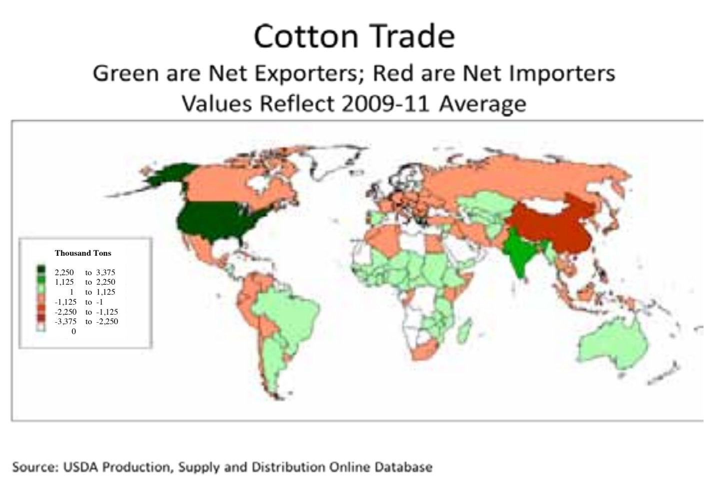


Figure 6: Cotton Seed Exports/Imports

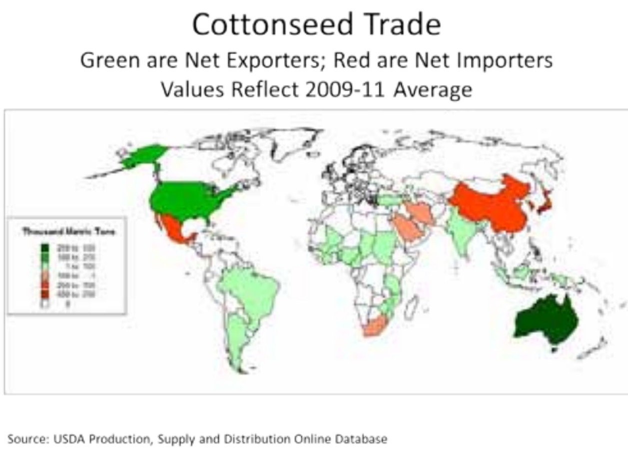
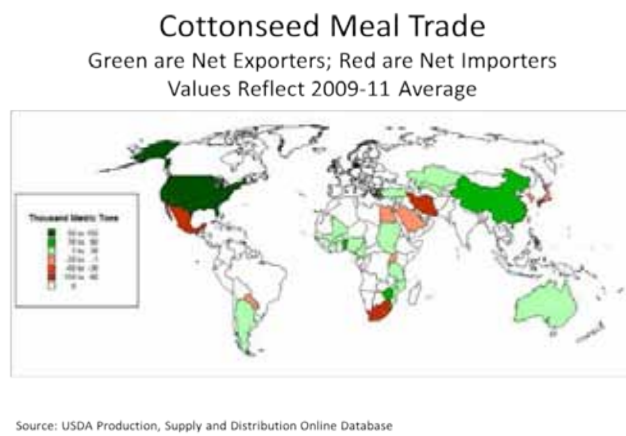


Figure 7: Cotton Seed Meal Exports/Imports



as a salad oil and an ingredient of mayonnaise, salad dressings, sauces, and marinades. As a cooking oil, it is used for frying in both commercial and home cooking. In this capacity, it is highly valued for its high smoke point (burning temperature) and its mild flavor especially in Asian stir frying. Cottonseed oil is rich in tocopherols, natural antioxidants, which contribute to its stability giving products that contain it a long shelf life. It is among the most unsaturated oils along with safflower, canola and sunflower seed oils.

The leading exporters of cotton seed oil are the U.S., Australia, and Uzbekistan followed by Argentina and Kazakhstan. The largest importer is Canada (Figure 8).

The end of the Multi Fiber Arrangement (MFA) and increased use of genetically modified (biotech) cotton have profoundly altered world cotton markets in recent years. The economic growth of China and India has also had an influence on world trade. During the mid-2000s, world cotton consumption grew at its fastest rate in decades and world cotton trade has grown even faster. The restructuring of world consumption and trade means that trade policies around the world are more important to U.S. cotton than perhaps at any time in the last 100 years (Clive James, 2011b).

Cotton fiber has not received the same scrutiny under domestic biosafety import laws as other major commodities have since most of these laws focus on food and feed. Even the European Union (EU), whose import laws for biotechnology are among the strictest, does not include cotton fiber.

Other cotton products – cotton seed, meal, and oil – are, however, subject to these rules. Fortunately, the percentage of these products in global trade is low compared to lint.

Table 2 presents world data in million metric tons for the four most recent seasons. As a percentage of exported cotton fiber, cottonseed, meal, and oil were 9.77%, 4.89%, and 1.88%, respectively, for the 2010/11.

Figure 8: Cotton Seed Oil Exports/Imports

The one exception to domestic regulations that include transgenic cotton fiber is Turkey. Turkey's new Biosafety Law became effective in September 2010. This law is probably the strictest among countries with biosafety regulations in place. Turkey is the only country that does not approve biotech crops for both food and feed. The law bans the cultivation of any biotech crops in the country, although it does make provisions for experimental field trials. Like other countries, it requires all biotech imports to be approved for use in Turkey and establishes a two-tiered testing regime in which all imports arriving from "risky origin countries" are tested unless the importer provides an analysis report from an accredited laboratory or a document from a government authority of the exporting country verifying that the shipment is biotech free or that the biotech product is among Turkey's approved events. These 27 high risk countries include the U.S., Argentina, Brazil, India, China, South Africa, Australia,

Table 2: World Supply and Distribution, Cottonseed Products (Million Metric Tons)

Product	2007/08	2008/09	2009/10	2010/11
Fiber, Production	26.07	23.46	22.17	25.10
Fiber, Exports	8.47	6.61	7.81	7.62
Cottonseed, Production	45.78	41.08	39.01	43.47
Cottonseed, Exports	0.81	0.56	0.59	0.78
Cottonseed Meal, Production	15.58	14.27	13.85	14.92
Cottonseed Meal, Exports	0.43	0.40	0.37	0.39
Cottonseed Oil, Production	5.21	4.77	4.62	5.00
Cottonseed Oil, Exports	0.16	0.15	0.10	0.15

Sources: ICAC and USDA Production, Supply, and Distribution Online Database

Mexico, Columbia, Philippines, Burkina Faso, Japan, South Korea, Canada, and the EU. Other imports are tested at a 10% rate. There is a zero tolerance threshold for the presence of unapproved biotech crops or products, meaning that even slight traces of unapproved biotech crops can make many agricultural products unmarketable in Turkey. Moreover, as of February 2012, Turkey had only approved 3 soybean and 13 maize events, while there are 56 events in global production and trade, making trade disruptions probable. Products containing 0.9% or more of biotech ingredients are required to be labeled; however, Turkey has yet to approve any events for food use. Biotech ingredients are banned in baby food and formulas as well as in food supplements for babies and young children. The law requires biotech products to be stored and processed separately, monitored, and tracked through the chain of commerce.

In the spring of 2011, cotton shipments into Turkey were being delayed at port. Earlier that year, the Ministry of Agriculture and Rural Affairs (MARA) was reorganized and the responsibility for the Biosafety Law was transferred from the Food Division to the Plant Protection and Control Division. The new person responsible for the oversight of the law reinterpreted the law to include cotton fiber. On April 2011, the port authorities were instructed to apply the Biosafety Law requirements to baled cotton lint.

After extensive consultation, the Plant Protection and Control Division sent a second memo to the port authorities explaining that the laboratories at the MARA determined that it is not possible to extract DNA from processed cotton fiber so that they could not definitively declare that the imported baled cotton lint was genetically modified or not.

Turkish cotton importers are now reluctantly signing letters of undertaking, which declares that their imports do not contain biotech cotton. This declaration is technically correct since the Turkish Biosafety Law defines a genetically modified organism (using biotechnology) as a living organism. The reluctance to sign these statements stems from the harsh penalties for violations of the law – fines of 10,000 to 200,000 Turkish lira (approximately US$5,000 to $100,000) and prison terms ranging from 3-12 years.

International Regulations and Biotechnology

There are a wide array of multinational bodies that have or claim a role is some aspect of the regulation of agricultural biotechnology and standard setting. Table 3 provides a list of these organizations along with their respective functions.

Of these, the Cartagena or Biosafety Protocol (BSP) is most specifically focused on biotech crops and bears directly on the trade of biotech commodities. It is an environmentally focused effort related to the transport and handling of living biotech materials across international borders. The Protocol is a product of the Convention for Biological Diversity (CBD), which resulted from a U.S.- sponsored U.N. resolution. A major environmental concern at the time was biological diversity or, more specifically, the concern that rapid loss of species around the world was occurring.

The Convention was unveiled during the Earth Summit in Rio de Janeiro in June 1992 with over

Table 3: International Institutions Involved in Agricultural Biotechnology

Institution	Purpose/Activity
Biosafety (Cartagena) Protocol	January 200 agreement under the U.N. Convention on Biological Diversity, on trans-boundary movements of Living Modified Organisms
Codex Alimentarius	Establishes science-based international food safety standards recognized by WTO in the Sanitary & Phytosanitary (SPS) Agreement. A task force of Codex has developed guidelines for assessing food risks of biotech crops
U.N. Food & Agriculture Organization	Interest in food security benefits of biotechnology vs. potential safety risks. FAO Commission on Genetic Resources for Food & Agriculture advises on availability and use of genetic resources for food and agriculture; equitable sharing of benefits – goals of the FAO Treaty on Plant Genetic Resources for Food and Agriculture
International Plant Protection Convention	Prevents spread of plant pests and pathogens. Its standards are recognized by the SPS Agreement
Organization for Economic Cooperation & Development	Consists of developed democracies. Fosters market economies and free trade. Promotes international harmonization of biotechnology regulations through development of consensus documents and information
World Health Organization	Oversees world trade rules now governed by the 1994 Uruguay Round Agreements including trade dispute settlement.

Source: Becker and Hanrahan, 2003

150 signatories excluding the U.S. There are two provisions of the Convention that have significant impact on international trade of biotech crops today. Article 8(g) of the Convention specifically requires nations "to regulate living modified organisms (LMOs) resulting from biotechnology which are likely to have adverse environmental impacts that could affect conservation and sustainable use of biological diversity, taking also into account the risks to human health."

Article 19, Paragraph 3 states: "The parties shall consider the need for and modalities of a protocol setting out appropriate procedures, including, in particular, advance informed agreement, in the field of the safe transfer, handling and use of any living modified organism resulting from biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity."

While still at Rio, four expert panels were assembled to identify those areas that were urgently in need of attention. It was determined that biosafety was a priority area for further regulation and they began to discuss the creation of a Biosafety Protocol pursuant to Article 19 of the CBD. For a more detailed description of the negotiation processes leading up to the Convention and the Protocol, see Saigo (2000).

The key provisions and related issues of the Protocol are as follows (Segarra and Fletcher, 2001):

- **Advance Informed Agreements**

  The BSP establishes the use of Advance Informed Agreements (AIA) between the importing and exporting parties that cover the first trans-boundary movement of genetically modified organism material (using biotechnology) intended for intentional introduction into the environment such as seeds for planting, fish for field release, and microbes for environmental remediation. Subsequent shipments are not subject to this procedure. The purpose of the AIAs is to ensure that recipient countries have the opportunity to assess environmental risks associated with the imported products. The exporter must provide a notification to the importing country including detailed information about the LMO, previous risk assessments of the LMO, and its regulatory status in the exporting country. The importing country must acknowledge receipt of the information within 90 days and its decision to allow the import, with or without conditions, within 270 days.

- **Risk Assessments**

  The BSP requires that decisions on proposed imports be based on risk assessments conducted in a scientific manner based on recognized techniques with consideration of advice and guidelines developed by relevant international organizations. The Protocol allows parties to use socioeconomic considerations in the decision to allow an import and allows the importer to require the exporter to conduct and finance the risk assessments as well as any mitigation measures. Confidential information obtained under BSP procedures must be protected by both importing and exporting parties, but the Protocol does not prescribe explicit liabilities for failures to protect intellectual property.

- **Precautionary Principle**

  The BSP codifies the precautionary principle in its preamble and in Articles 10 and 11, which describe trading procedures for importing parties. Although risk assessments and risk management are prominent features of the Protocol, these articles state that in the lack of scientific certainty, importers could deny entry to undesired biotech materials. In general, most interpretations agree that the precautionary approach encourages policy makers to err on the side of caution when facing scientific uncertainty. Proponents of this approach claim that it is a temporary means to allow for further scientific inquiry. Critics of the approach worry that it may promote false expectations and the demand for zero risk and that it can be used, at its worst, as a form of disguised protectionism.

- **Notification/Labeling**

  The Protocol establishes mandatory entry notifications by exporting countries to the competent national authority in importing countries about incoming shipments. Bulk shipments of biotech commodities must be accompanied by documentation stating that such shipments "May Contain" GM material and that they are "Not intended for intentional introduction into the environment" in lieu of a formal AIA. This provision only applies to biotech shipments intended for food, feed, or processing.

- **Biosafety Clearinghouse**

  The Protocol established the Biosafety Clearinghouse (BCH) as a website administered by the Secretariat to the Convention as a vehicle to share scientific, environmental, and legal information on biotech materials. The BCH is a centralized source for information on national laws, guidelines, and regulations of the BSP. The BCH website can be viewed at http://bch.cbd.int.

- **Capacity Building**

  The BSP promotes international cooperation to help developing countries acquire resources and knowledge to use biotechnology safely and to develop efficient regulations. It encourages member governments to assist with scientific and technical training to promote the transfer of technology, information, and financial resources.

- **The Savings Clause**

  One of the most contentious issues in developing the BSP was to determine how the Protocol would relate to other bilateral or international trade agreements, notably those under the World Trade Organization (WTO). A compromise position was reached by including a "savings clause" in the preamble that states, "nothing in the Protocol implies a change in the rights and obligations of governments under the WTO or other existing international agreements." Confusingly though, the preamble also states that the BSP will not be subordinated to other international agreements and that they should be mutually supportive.

Current Obstacles to Trade of Agricultural Biotechnology

Public acceptance

One obstacle to international trade of biotech crops has been the differences in public acceptance of these crops, which have resulted in a variety of different regulatory systems. There has been considerable public debate in importing countries in Asia, the EU, and elsewhere over the safety and desirability of biotech food and feed. This debate has probably been most intense, and fueled by anti-biotech groups like Greenpeace, in the EU. This debate culminated in June 1999 with the EU formally imposing a moratorium on approvals of any additional biotech crops.

On the other hand, U.S. consumers, for the most part, are neutral to positive towards the technology. In May 2012, the International Food Information Council released its latest survey of U.S. consumers on their attitudes toward food safety (http://www.foodinsight.org). The survey found that, by and large, perceptions of food technology have remained steady, despite increased coverage of food technology and modern food production issues in the media. Most consumers are favorable toward various benefits offered through plant and animal biotechnology, especially those that may have a positive impact on their health and/or the environment. Concern over biotechnology ranked at 8 of 10 issues raised with only 2% of respondents expressing concern - unchanged for IFIC's 2010 survey. Leading concerns included disease contamination, handling and preparation, and preservations and chemicals. It has been speculated that this attitude reflects a confidence by the U.S. consumers in the current regulatory oversight. This is not to say that there has not been opposition in the U.S. Anti-biotech groups such as Friends of the Earth and the Union of Concerned Scientists have pressured companies into removing biotech ingredients from branded food products including baby food (Gerber), snack foods (Frito Lay), and french fries (McDonalds). There is currently a referendum underway to require the labeling of biotech foods and ingredients in California. Sheldon (2001) explores in further depth the underlying reasons for these differences in acceptance.

The EU, on the other hand, has been very apprehensive about the technology and has developed the most stringent import regime worldwide. It is founded on the precautionary principle, the precept that an action should not be taken if the consequences are uncertain and potentially dangerous. Applications for the approval of transgenic crops for release into the environment and even for entrance into the food or feed market must be accompanied by a full risk assessment which must identify and evaluate potential negative effects both direct and indirect as well as consideration of the cumulative and long-term effects on human health and the environment. Approvals are legitimate for ten years, after which the applicant must submit an application for renewal. The regulations include requirements for product labeling irrespective of whether biotech material can still be detected after processing e.g. highly refined cotton seed oil. There are also mandates for traceability, monitoring, and labeling throughout the market chain. Furthermore, in July 2010, the European Commission granted member states the authority to allow, restrict or ban the cultivation of biotech crops on part or all of their territory. Many EU countries ban the cultivation of biotech crops but, in 2011, six EU countries (Spain, Portugal, Czech, Poland, Slovakia and Romania) planted a record 114,490 hectares of biotech Bt maize, a substantial 26% higher than 2010, with Spain growing 85% of the total in the EU with a record adoption rate of 28% (ISAAA Brief 43-2011).

Responding to domestic public opinion, national regulatory systems have adopted widely divergent approaches to regulating biotechnology. These systems vary in the extensiveness of the required dossiers, in the time needed for approvals, labeling, and thresholds for unapproved materials. For instance, in the U.S., Canada, Japan, and Taiwan, food with up to 5% of approved biotech ingredient can be classified as "non-biotech" while in Australia, New Zealand, South Africa, Brazil, and China, the threshold is 1%. In the EU, all food with more than 0.9% approved GMO (biotech) material must be labeled as "GMO" (Stein and Rodriguez-Cerezo, 2010a).

Asynchronous approvals and low level presence

With a patchwork of various regulatory regimes in place, it not only makes it very difficult for the exporter, it can and has been very costly. Shipments have been rejected at port for including small amounts of biotech material that has not been approved in the importing country. Low level presence (LLP) is the unintentional presence of a transgenic event(s) that has undergone a full risk assessment and authorization in one or more countries but not in the country of import. LLP is the result of asynchronous approvals (AA) among trading partners. AA may arise from differences in national regulatory processes and requirements as well as their pace of approvals.

Kalaitzandonakes (2011) identifies four different types of unauthorized transgenic events:

1. Those that have received regulatory approval for some uses (e.g. feed) but not for others (e.g. food). The Starlink® maize incident is an example;
2. Events that have been approved for all possible uses in one or more countries but not yet in others (asynchronous approval);
3. Experimental events contained in laboratories, greenhouses, and field trials that are unexpectedly found in the food/feed supply (Liberty Link rice). Such events are usually still in development and have not been approved by any country;
4. Events that have received a time-limited approval that may have expired (EU regulations).

Grains and oilseeds predominant international trade flows of biotech agricultural products. They are also bulky and relatively expensive to transport and store while their value per unit is relatively low. Grain handlers must minimize operational costs and maximize efficiencies in order to make trade possible. One means to achieve such goals is through aggregation or co-mingling where grains from numerous farms and storage facilities are continually mixed throughout the supply chain. Such co-mingling in bilateral trade where AA is involved, will inevitably lead to LLP and trade disruptions, particularly if the importing country embraces a zero tolerance for LLP. The exporter will then be forced to segregate unauthorized events. When such segregation is not feasible or too costly, trade is suspended between the two countries. In such an event, the exporter will lose a market and the importing country will experience higher grain and food prices (Kalaitzandonakes, 2011). Shippers also incur additional costs for testing, shipment rejections, and demurrage when such trade disruptions occur.

There have been several cases of trade disruption due to LLP, and the costs are high. The EU moratorium caused a de facto ban of U.S. maize imports and was costly to European importers. In order to import maize, EU countries were forced to source from Brazil, after other sources were exhausted, with a reported premium of 50-70 euros per ton over U.S. maize. Similarly, with the unintentional introduction of experimental rice, LL601, into the rice supply chain in the U.S., the EU and others banned U.S. rice, which cost approximately 3.5-7.5 million euros per rice importer (Gruere, 2009).

When Turkey's biosafety law went into effect, it effectively stopped sales of U.S. grain from February to May 2011. The price of animal feed increased to very high levels until new non-biotech markets were established and the government made some biotech approvals.

China's regulatory infrastructure is still developing, and includes biosafety regulations that present serious market disruption potential such as inadequate protection for intellectual property rights, a zero or low level presence threshold, and a lack of policy on stacked events. Moreover, China presents a unique impediment to international trade of biotech commodities in that it is the only country that requires that a product be fully approved in the originating country before an application can be filed for approval in China. Furthermore, the Ministry of Agriculture (MOA) which is responsible for approving imported biotechnology products requires authorized domestic institutions to conduct environmental safety (field trials) and food safety (animal feeding) tests to verify data provided by the technology provider. The National Biosafety Committee must review all these documents, including reports generated from verification tests, before MOA can issue a biosafety certificate. In general, the process of getting a biosafety certificate for imported biotech food crops for processing will last about two years. Such a lengthy disparity in approval along with China's major importing role creates a significant opportunity for trade disruptions (Lagos and Bugang, 2011).

International trade of biotech commodities will become more complex as the capacity to develop such products expands. Currently, the majority of the technology comes from private companies in the U.S. and decreasingly from Europe. In coming years, more biotech crops will be supplied by private and public entities from Asia, particularly China and India, and may present other consequences. In Asia, biotech crops are usually developed for domestic use and consumption rather than for export and are less likely to be submitted for approval in other countries. Trade disruptions due to this "isolated foreign approval" or asymmetric approval could become more common (Stein and Rodriguez-Cerezo, 2010a). In Latin America, Brazil and Argentina have greatly expanded their acreage of biotech crops. Brazil has streamlined its regulatory system and is encouraging companies to develop new transgenics. Even in emerging economies, technology transfers from developed countries could increase the acceptance and adoption of biotech crops in those countries. If so, the number of alternative suppliers of non-biotech commodities would decrease, making it more difficult for importers to simply redirect trade flows. Africa has shied away from the technology in the past due to the fear of market disruptions with its largest trading partner, the EU. Some African countries are reconsidering that stance and some are eager to embrace the technology.

Asynchronous approvals may be further exacerbated by the development of multiple transgenic traits ("stacks") within a crop. Stacks can be developed through traditional breeding of transgenic parents or through additional transformation. These crops are becoming more popular as a means of resistance management and more complete pest control. With the various combinations of traits that are possible, the number of potential stacks can quickly become overwhelming and could backlog regulatory systems. For example, the EU and some other countries require the stacked biotech crop to go through the regulatory system as a new biotech crop, irrespective of whether the parental biotech events were already authorized or not.

Although trade disruptions due to AA and LLP will probably never be eliminated, there are certain activities that governments, technology providers, and shippers can do to reduce their occurrences. Technology providers can make certain that approvals are completed in countries that are major and important markets for the biotech crop prior to commercialization. In 2007, U.S. technology providers have voluntarily developed and agreed to the Product Launch Stewardship Policy which includes, among others, the following procedures (http://www.bio.org/articles/ product-launch-stewardship-policy):

- Conduct a market and trade assessment to identify key import markets prior to the commercialization of any new biotechnology product in any country of commercial launch. In that market and trade assessment, consult at an early stage with the value chain for the specific crop;
- Meet applicable regulatory requirements in key markets, which at a minimum include the United States, Canada, and Japan prior to commercialization of a new biotechnology product.

Handlers and shippers must be aware of current asynchronous approvals and use testing at different parts of the commodity flow, but most frequently, when there is a change in custody. Testing at port of origin is important; in cases where an unapproved event is detected, the shipment can be redirected prior to transport.

Governments can assist in this problem by diminishing the time gaps between national and international approvals so that AA's are reduced. Governments can streamline their approval processes through an abbreviated risk assessment for health and/or environmental risks especially for events that have a long history of safe use, such as Bt and herbicide tolerance.

The most effective means for government assistance, however, would be the establishment of a national LLP tolerance policy. A tolerance is either a set percentage of LLP that will be accepted or, as in the U.S., the acceptable tolerance is set on a case-by-case basis and according to the risk presented by the event. The lower the tolerance is set, the more trade disruptions will occur. A zero tolerance policy is not practical as it has been seen where soybean shipments have been rejected in Europe because of the detection of maize dust. As stated earlier, the continuance of a zero tolerance policy will likely result in cessation of trade between countries. An economic impact analysis of LLP policies is presented by Kalaitzandonakes (2011).

In response to the LLP issue, in July 2008, the Codex Alimentarius Task Force on Foods Derived from Biotechnology presented an international guidance for food and feed safety assessments of biotech events. The Annex on Food Safety Assessment in Situations of Low-level Presence of Recombinant DNA Plant Material in Food, commonly called the "Codex Annex", aims to encourage countries to adopt simplified and quicker procedures for any new biotech event to be approved temporarily at low levels prior to completing its full approvals. It is a flexible document that distinguishes different categories of products such as processed products, biotech grains whose fraction is small in final consumer products, and fruits and vegetables. It does not, however, specify whether the rule should apply to each category in the same manner. More importantly, it provides to the country the discretion to define its own LLP.

The standard was rapidly adopted by the more than 160 members of the Codex Alimentarius, despite some country differences. Its acceptance is viewed as a sign of international recognition on the increasing importance of LLP in trade and the necessity for practical solutions to respond to this reality. In comparison, discussions at the Codex Alimentarius Committee on Food Labeling for genetically modified food (using biotechnology) has remained unresolved for years due to irreconcilable differences among states.

Similar efforts to develop guidelines for a streamlined environmental risk assessment have been developed by an OECD task force. The guidelines are meant to complement the Codex Annex and focuses on biotech seeds and commodities that are able to propagate (Gruere, 2009; Kalaitzandonakes, 2011)Across the globe, more and more farmers are deciding to utilize biotechnology for higher yields and reduced production costs. Farmers have adopted crops genetically modified through modern biotechnology with the fastest adoption rate of any crop technology. The primary biotech crops grown in the U.S. are maize, cotton, and soybeans with an average biotech adoption rate of around 90%.

Consumer acceptance of biotech crops has varied greatly around the globe. In the EU, resistance to the technology has been high, yet, it is not an issue of concern for U.S. consumers. This range of acceptance has led to a patchwork of different domestic biosafety laws which govern the imports of biotech commodities, products, and seed.

Within these biosafety laws, cotton fiber has not received the scrutiny as have the other major commodities since most of these laws focus on food and feed. Even the European Union (EU), whose import laws for biotechnology are among the strictest, does not include cotton fiber.

Other cotton products – cotton seed, meal, and oil – are, however, subject to these rules. Fortunately, the percentage of these products in global trade is low compared to lint. However, when export markets are important for these products, biosafety laws can prove to be an impediment to trade.

Low level presence of an unapproved event is the result of asynchronous approvals and is the major impediment to free flowing trade in biotech commodities. The most effective means to relieve this problem is for governments to establish a national LLP tolerance policy harmonious with other countries.

Biotech Cotton: Perspectives from the Field

Compiled from reports by
Paulo A. Vianna Barroso and Lúcia Viera Hoffmann, Brazil;
Eduardo Roman and Luz Amparo Fonseca, Colombia;
Tassawar Hussain Malik, Pakistan;
and Hennie Bruwer, South Africa

In the late 1990's, biotech cotton varieties were introduced into Brazil, Columbia, South Africa, and Pakistan where they were readily adopted. Biotech cotton was not formally deregulated by the government of Pakistan for commercial cultivation until 2010.

Benefits

According to Barroso and Hoffmann, adoption of biotech cotton has been less widespread in Brazil, indicating that the benefits of the technology are not universal. The effectiveness of biotech cotton in Latin America is lower than in other cotton growing regions. Although lepidopterans are very important in South and Central America, boll weevil is still the key pest in most of the countries in these regions, and the Cry insecticidal proteins present in Bt cotton do not affect weevils and other sucking pests. The benefits observed in Africa, Asia, and the USA will only be achieved in Brazil if boll weevil resistance is incorporated. Actions to develop boll weevil resistance as an important regional biotech cotton trait are ongoing in public research institutes of Brazil and Argentina. Boll weevil is not present in all cotton growing regions, unlike the lepidopterans, and a smaller market demand may hinder global companies from investing in this trait.

Pakistani cotton is plagued with a phytolethal virus disease known as Cotton Leaf Curl Virus (CLCuV) in both traditional and modern biotech varieties. This virus has curtailed the adoption of biotech cotton by farmers because a successful crop in the presence of the CLCuV is always questionable. Farmers need CLCuV tolerant varieties and eradication of this disease to ensure the achievement of economic cotton production and, then, it would be expected that adoption of biotech cotton technology would increase.

South African farmers have benefited from the introduction of biotech cotton. However, adoption of the technology has been inhibited because of lower world cotton prices, cheap textile and garment imports, and higher comparative prices for competing crops like maize, soybeans, and sunflower seed. The technology has increased productivity but has not yet made South Africa competitive in the world market.

Table 4: Average Cotton Yields in South Africa

Production Year	Irrigated Yield (Kg/ha)		Rainfed Yield (Kg/ha)	
	Seedcotton	Lint	Seedcotton	Lint
1997/98	2,724	1,008	580	215
1998/99	2,680	992	545	202
1999/00	3,107	1,150	777	287
2000/01	3,455	1,278	593	219
2001/02	3,538	1,309	515	191
2002/03	3,482	1,288	475	176
2003/04	3,455	1,278	492	182
2004/05	3,791	1,403	521	193
2005/06	3,633	1,344	485	179
2006/07	3,674	1,359	541	200
2007/08	4,067	1,505	825	305
2008/09	4,329	1,602	757	280
2009/10	4,865	1,800	712	263
2010/11	3,931	1,454	715	265
2011/12*	4,433	1,640	637	236

* Provisional

Similar benefits of transgenic cotton traits were reported for each country – increased yields due to enhanced pest control, increased populations of beneficial insects which in turn suppressed other pest populations, reduced input and labor costs, increased farmer profits, and environmental benefits such as reduced tillage.

Brazil reports that in its experience, there is a "halo effect" - an indirect effect resulting in a reduction of the pest population in non-biotech crop fields near biotech cotton fields. The logic of the effect is simple: part of the females emerging from non- biotech crops lays their eggs on biotech crops and the larvae emerging are not able complete their life cycle. Consequently, there is a reduction of the total pest population in regions where insect resistant biotech cotton is prevalent. Very significant halo effects were described for pink bollworm in Arizona (USA) and in six provinces of the Yangtze River Valley (China). A similar effect was also reported for cotton bollworm in some regions of China. As cotton bollworm is a generalist pest, the effect was not only in non- biotech cotton but also in other crop species.

Secondary Pests

Each country also reported some type of negative or unintended consequence of transgenic biotech cotton production over time. The most common problem is the rise in importance of secondary pest. As pesticide applications for the target Lepidopteran species declines, secondary pests, which had previously been inadvertently controlled by applications of chemical insecticides, have increased in numbers to become primary pests.

In Colombia, secondary pests include aphids (*Aphis gossypii*), mites (*Tetranychus* spp.), bug manchador (*Dysdercus* spp.), beetle (*Cyclocephal*a spp.) and, one of the most important worldwide, whitefly (*Bemisia tabaci*). Economic damage thresholds and field sampling methodologies for these pests either do not exist and must be developed or are outdated and need to be updated.

Columbia also reported that the incidence and severity of diseases, particularly ramularia (*Ramularia areola*), anthracnose (*Colletotrichum gossypii*) and boll rot (disease complex), is higher in biotech cotton than in conventional cotton varieties. In fact, since 2006, multiple chemical treatments have been needed to manage these diseases. This situation has generated the need for research to identify options for management and control of these pathogens. It is not clear at this point whether the increased incidence of disease is due to inoculum present on the seed coming into the country from the US and Australia or if the transgenic varieties are more susceptible. Another factor could be the different canopy of the biotech cotton. The biotech cotton varieties that have entered the country perform differently than native Colombian varieties. Farmers have adjusted their population densities resulting in a more dense leaf canopy. Denser canopies may be creating microclimates that favor the emergence and development of diseases, as well as hindering the effective applications of agrochemicals to control insect pests.

Resistance Management

All countries reported high levels of concern about the development of resistance in the targets pests. The use of refuges to delay or inhibit resistance is mandatory in some countries, including Brazil, the US, and Australia, but not in other countries. In Columbia, there are mandatory refuge requirements of either 20% non-transgenic cotton, which can be sprayed with pesticides that do not contain Bt as an active ingredient, or a 4% non-transgenic refuge that cannot be treated with any pesticides.

A second strategy for insect resistance management is the use of biotech cotton containing more than one insecticidal protein, provided that the proteins have different modes of action within the target insects. As resistance genes in insect populations occur in low frequencies, the probability of the simultaneous presence of both genes in an individual is substantially reduced. Associated with these resistance management strategies, it is imperative that pest populations be monitored for early detection of increased tolerance of the Bt toxin by the insect pests and to permit the implementation of mitigation measures early enough to prevention the development of resistance.

Lack of Compliance and Adapted Varieties

Columbia and Pakistan report the need for transgenic varieties that are suitable for local growing conditions. In Columbia, there are three distinct agro ecological zones each with a long history of cotton production. It was proposed that the introduction of new varieties should occur only after multiple agronomic field trials, including trials with differing planting dates, in each of the cotton regions are completed and analyzed to determine which are the most suitable for Columbia's diverse growing conditions.

Pakistan reports that the lack of cotton varieties with high yield potential and acceptable fiber quality is the major concern of Pakistani growers. The technology currently only provides protection against certain pests. Production potential still depends upon the yield potential of the transformed variety. Hence, breeding and development of varieties with increased production ability is of prime importance in Pakistan. In Pakistan, there is a flood of "novel" cotton varieties. Breeders from the public and private sectors are continually introducing immature and heterogeneous material as new varieties to farmers. The material with poor genetic uniformity results in questionable trait purity and affects overall crop protection against the major target pests. Now there has been an increased awareness among farmers. The Pakistan Central Cotton Committee has launched Bt test trials in four independent labs for independent evaluations of purity and toxin levels of candidate biotech cotton varieties. Most of the indigenously developed biotech cotton varieties tested during the last few years have shown a low and sub-standard expression of Bt toxin. Breeders and biotechnologists have been asked to improve the Bt toxin level of their varieties to an effective dosage level. Breeding genetically uniform varieties following standardized breeding protocols and improving Bt expression may resolve the concerns of Pakistani cotton farmers. Growing varieties with low Bt expression is not only uneconomical for farmers but may also encourage the development of resistance in the insect pests.

Early maturity is another desirable trait for Pakistan since the existing cotton varieties are of medium to late maturity. The biotech varieties were adapted to early sowing (February-March) instead of normal sowing (April-May). The shift to earlier planting biotech cotton has seriously disturbed the growers in some parts of the cotton belt especially the non-traditional cotton areas in terms of the traditional rotations under practice. In some cases, early sowing encouraged early infestations of sucking pests and increased the cost of chemical control. Farmers in Pakistan need earlier maturing varieties so that traditional crop rotation systems are not disturbed. Pakistan also reported that farmers frequently complain about poor germination rates and vigor of transgenic cotton varieties.

Future Prospects

Cotton farmers around the globe anticipate the commercial availability of a range of new biotech traits. It is also important to develop biotech cottons to assist in the solution of other phytosanitary problems spread worldwide such as Fusarium and Verticillium wilt as well as important regional pests and diseases, markedly boll weevil in Latin America and Cotton Leaf Curl Virus in Pakistan and India. More traits must also be developed through biotech technology to increase yield, improve nutrient use efficiency, and enhance the tolerance to abiotic stress such as salt, drought, and temperature. Facilitation of the introduction of new biotech traits will involve greater cooperation among the multinational technology companies, state governments, local research facilities, and farmers. Governments must adopt science-based and predictable regulatory regimes to create a healthy business environment for both national and international companies. Local research is needed so that transgenic varieties suited for local growing conditions can be developed. Finally, farmers and consumers need to be educated about the technology. A more conducive framework will foster the introduction of new technologies, which will benefit farmers, consumers, and the environment.

Upstream Technologies

Keshav Kranthi, India

Recent advances in biotechnological research have facilitated tremendous progress in cotton crop improvement for economically important traits, especially where conventional plant breeding approaches faced limitations such as non-availability of the desired trait in the germplasm pool and also problems related to undesirable linkage drag. There has been an all round development in all spheres of science that range from new methods of plant breeding, The Quantitative Trait Loci (QTL) analysis, isolation of markers, genome sequencing, new bio-pesticides, new genes for pest management, new methods of pest control such as RNAi (RNA interference) based transgenic crops and new generation pesticides.

Biotechnology uses in agriculture represented a breakthrough in agricultural sciences. With the advent of genetic engineering technologies, plants could be modified precisely with the desired traits very rapidly with great accuracy. Several biotech varieties of crops were developed to resist insect pests, diseases and herbicides. Biotech crops are rigorously subjected to biosafety tests and agronomic traits as prescribed by the concerned regulatory authorities in each country, before approval for commercial cultivation. The use of biotech crops, in appropriate circumstances, can have considerable potential for improving agriculture and the livelihood of poor farmers in developing countries.

Insect resistant biotech cotton with cry1Ac was first released in the USA, Mexico and Australia during 1996. Later it was released in China (1997), South Africa (1998), Argentina (1998), India (2002), Colombia (2002), Brazil (2005), Costa-Rica (2008), Burkina Faso (2009) and recently in Pakistan and Myanmar in 2010 and Sudan in 2011. Currently an estimated 23 million hectares are under biotech cotton in 13 countries. This accounted for almost 69% of the total global cotton area in 2011/12. India is leading in biotech cotton acreage with about 10.5 million hectares at an adoption rate of 82%.

Resistance to Biotic Stress

The recent advances made in transgenic research over the past decade and the advent of insect resistant transgenic crops, have opened up new possibilities, new areas of research and new avenues in eco-sustainable pest management. A few recent examples deal with the use of genes encoding insecticidal toxins from the bacteria *Bacillus thuringiensis*, from nematodes, *Xenorhabdus* and *Photorhabditis*, and hormones from insects, allatotropins, allatostatins, proctolin etc. alarm pheromone sesquiterpene (*E*)-farnesene (*E*f) and proteinase inhibitors and lectins from plants that have a significant effect on several insect species.

Biotech cotton based on the insecticidal genes from *Bacillus thuringiensis* has been successfully used in at least 13 cotton growing countries to combat bollworm infestations. However, it is important to strengthen biotechnology with additional genes through gene stacking to ensure long term sustainability. There are several sources in nature that have been used to isolate insecticidal genes. Genes from endo-symbiotic bacteria of nematodes, *Xenorhabdus* and *Photorhabdus* have been actively considered for the development of transgenic crops. Amongst animal sources, anti-chymotrypsin, anti-elastase, chitinase, cholesterol oxidase and anti-trypsin were isolated from the tobacco hornworm, *Manduca sexta* and used to develop biotech cotton resistant to sucking pests and lepidopteran insects. Trypsin inhibitors and spleen inhibitors isolated from cattle, protease inhibitors from plants (Soybean, Barley, Cowpea, squash, mustard, rice, potato, tomato), amylase inhibitor genes from beans and cereals and lectins from plant sources have been used to develop biotech crops resistant to insect pests. Other genes include *chitinases, glucanases, peroxidase* and *tryptophan decarboxylase* from various plant sources to develop insect and disease resistant cotton. Replicase genes and coat protein genes have been used to develop leaf curl virus resistant varieties through over-expression of the proteins or silencing of the genes through RNAi, especially for countries in Africa, India and Pakistan where the cotton leaf curl virus (CLCuV) problem can cause severe economic losses.

Insect behavior is guided by semiochemicals (pheromones) called allomones and kairomones. Plants emit chemical signals under stress. Signal transduction pathways in cotton are interspersed with many chemical signals including ethylene, jasmonic acid and several related volatiles. Genes that control interaction between insects and plants can be effectively manipulated to disrupt insect-plant relationships and thereby reduce damage to crops. It has now been proven that new biotech crops that scare insects can be developed. Insects release chemicals called alarm pheromones when their enemies scare them. This warns their colonies to escape. New biotech crops express alarm pheromones that scare the specific insect pests. The alarm pheromone for many species of aphids, which causes dispersion in response to attack by predators or parasitoids, consists of the sesquiterpene (*E*)-farnesene (*E*f). High levels of expression in *Arabidopsis thaliana* plants of an *Efsynthase* gene cloned from *Mentha piperita* were used to cause emission of pure *E*f (Beale *et al.*, 2006). These plants elicited potent effects on behavior of the aphid *Myzus persicae* (alarm and repellent responses) and its parasitoid Diaeretiella rapae (an arrestant response).

The possibilities of discovering new genes for pest management have expanded into infinity, with the introduction of new concepts such as gene silencing through RNA interference (RNAi). RNAi deploys double stranded RNA (dsRNA) to silence specific endogenous genes in the target organism, which can be specific to the class, genus or even the specific target species. Thus, crucial species-specific genes of insect pests are being identified, along with the dsRNA expressed in plants to control them. Gene silencing has been used to develop a new biotech cotton variety that specifically controls bollworms by silencing a gossypol degrading enzyme called CYP6AE14 which otherwise enables bollworms to survive on cotton (Mao *et al.*, 2007). When a bollworm eats the double stranded RNA (dsRNA) of the *CYP6AE1*4 gene, the enzyme is silenced and undigested gossypol remains in the stomach and kills larvae. The technology has immense potential in pest management that can be sophisticated to the extent of being extremely specific for the control of target pests alone.

RNAi (RNA interference) based gene silencing technology is being explored through biotech strategies to develop insect and disease resistant varieties. Important diseases such as the cotton leaf curl virus and bacterial blight can be effectively managed by biotechnology applications including RNAi by pyramiding native resistance available. Similarly, efforts are being made to identify 'pathogen species specific' genes present in the pathogen species and 'insect-species-specific' genes present in the insect gut which are functionally important for feeding, digestion and other biological activities. There is a need to identify effective siRNAs and/or miRNAs and their targets. Gene sequences and the novel structures are being explored for their utility for crop protection through conventional or transgenic approaches for the management of cotton insect pests such as the bollworms, jassids, whiteflies and new pests.

Herbicide resistant biotech cotton in small-scale production systems has been found to be user-friendly, effective and profitable. However, herbicide tolerant cotton should find a useful place in small scale farming systems only with careful planning to ensure alternative placement of intercrops to avoid the direct effect of herbicide drift and also to ensure that cotton does not become the sole crop in a production system. Biotech cotton varieties resistant against the leaf curl virus disease have not yet been released commercially and have immense potential in India and Pakistan, where the disease is a major problem. Efforts are being made to develop drought resistant cotton varieties through recombinant DNA approaches. Such biotech products may help vast tracts of rainfed cotton cultivation.

Resistance to Abiotic Stress

Though cotton is a drought tolerant crop by nature, undesirable stress either due to water logging at vegetative phase or moisture stress at reproductive phase or prolonged drought during sowing time or reproductive phase, or high saline conditions can severely debilitate the crop. Climate change can adversely affect adaptability levels of varieties that were carefully selected and developed by farmers and plant breeders over the past several years to suit specific agro-ecological conditions of specific cropping zones. It is necessary to identify, classify and categorize germplasm lines that have unique traits to withstand cold, heat, high CO_2, and other stresses that are envisaged to occur with climate change.

Cotton farming has been extended into marginal ecosystems in the rainfed tracts of many parts of the globe. In these fragile ecosystems, soil nutrient status is very poor. To realize potential yields, large amounts of fertilizers will be needed to meet crop demands, and because of poor transportation infrastructure, fertilizer supply is not always guaranteed. There is a growing concern about environmental pollution because of farming (increased carbon emissions through burning and oxidation of organic matter, pollution from fertilizers and pesticides contaminating the ground and surface water, and excess irrigation causing land degradation through salinization, and other concerns). Some large tracts under cotton are under saline soils, or under saline water use. Biotech approaches can accelerate the development of varieties resistant to abiotic stress.

Genomics, proteomic and metabolic studies have un-raveled the relative roles of several genes in combating abiotic stress in cotton. Several drought related genes have been cloned and characterized in recent times. Zhang *et al.*, (2009) reported on the nine ESTs including *photosystem I psaH protein*, and *H+-ATPase* related genes that were up-regulated at different levels in drought stress cotton seedlings. These genes are responsible for the absorption and utilization of water through adjusting the photosynthesis process. Under drought stress the two genes were found to be highly induced. cDNAs differentially expressed in response to drought stress also revealed the role of *CaLEALI* gene in response to various abiotic stresses.

Rodrigues *et al.* (2011) conducted microarray analysis and identified 720 salt-responsive genes, of which 695 were down regulated and only 25 were up regulated in the salt tolerant bulk. Gene ontology of annotated genes revealed that at least some of the identified salt responsive transcripts belong to pathways known to be associated with salt stress including osmolyte and lipid metabolism, cell wall structure, and membrane synthesis. Recently Park *et al.* (2012) identified a total of 519 differentially expressed transcript derived frabiotechents in stressed cotton plants. Of these, 147 transcript derived frabiotechent sequences were functionally annotated according to their gene ontology. They found heat shock protein-related and reactive oxygen species-related transcript derived frabiotechents to be among the major parts of functional pathways induced by water deficit stress. Also, twelve novel transcripts were identified as both water deficit responsive and cotton specific. The study demonstrated complex mechanisms involved with polyploid cotton's transcriptome response to naturally occurring field water deficit stress. The genes identified can be used as candidate targets to manipulate the water use characteristics of cotton at the molecular level.

A few years ago attempts were made to develop biotech cotton for abiotic stress-tolerance, through the deployment of genes that are responsible for modification of a single metabolite that would confer increased tolerance to salt or drought stress. Stress-induced proteins with known functions such as water channel proteins, key enzymes for osmolyte biosynthesis of betaine, proline, trehalose, and polyamines were the initial targets of plant transformation. Drought responsive element binding proteins (DREB) *rd29A* genes for drought, high-salt & cold stress have been identified and used in several crops including cotton. Superoxide dismutase (SOD) confers chilling stress and is being explored for its utility in cotton. Transgenic approaches provided proof of concept of the relevance of many genes such as P5CS, *Glyoxalase AHK1/ATHK1, DREBs, PDH45Helicase, NPK1, DREB2 like small protein such as CAP2, BiotechDREB2, AtHARDY, ARAG* etc., which mainly addressed cellular level tolerance in model plant species, need to be utilized in cotton. Along with the improvement of primary constitutive traits such as root growth (*Alfin, AUX1, PIN-1, NAC-1*), Wax (*SHINE / WIN1, WXP1/ WXP2)* associated traits can be included using transgenic approach. A combination of the above traits in a coordinated manner will help to obtain cotton genotypes with better adaption to climate change, particularly abiotic stresses. Recently Hozain *et al.* (2012) reported that ectopic expression of a gene AtSAP5 (*Arabidopsis thaliana* stress associated protein) AtSAP5 that encodes proteins containing A20/AN1 zinc finger domains, under CaMV35S promoter resulted in up-regulation of putative stress-responsive genes in transgenic cotton such as a small heat-shock protein gene (*GHSP17.6*), a gene encoding galactinol synthetase 2 (*GhGolS2*) involved in osmoprotection, and two genes (*GhUGT73B5* and *GhUGT73C6*) encoding UDP-glucose glycosyltransferase, and showed complete protection of photosystem (PS) II complexes from photodamage. Transgenic cotton also showed tolerance to moderate heat stress. Drought tolerant transgenic cotton may be developed by utilizing *AtSAP5* gene driven by drought inducible promoters.

Cotton is sensitive to photoperiod and thermal conditions and does not adjust easily to new environments. Genetic manipulation of Rubisco activase can alter photoperiod and thermal sensitivity to enhance the adaptability of cotton to a wider range of environments. The maintenance of a positive carbon balance during stress is important to avoid a yield penalty. Plants respond to different environmental cues through signal perception and transducing the signals to combat stress. The phenomenon can be elucidated through functional genomics. Physiological efficiency of the cotton crop can be improved by changing the C_3 pathway to be more towards the C_4 pathway. Cotton being a C_3 crop, genetic manipulation to maintain positive carbon balance either by increasing carboxylation reaction or by decreasing photo respiration will enhance the water use efficiency (WUE) and nutrient use efficiency (NUE), thereby enhancing yields. Single cell C_4 mechanism suggests possibilities to express C_4 genes in C_3, recent progress in cloning and expression provides leads for the coordinated expression of relevant genes in target organelles. Recent successful demonstration of increasing CO_2 (CCM) and biomass in Arabidopsis by utilizing decarboxylation of glycolate (a pathway that exists in bacteria) acts as an option for improvement of C_3 crops such as cotton.

Biotech Research for Fiber Quality Improvement

Classical breeding approaches have been efficiently used over the past several years to improve fiber quality. The recent progress in molecular aspects of fiber development has added new dimensions to plant breeding approaches. Currently, attempts are being made to unravel the process of cotton fiber development step by step and identify the genes involved in determining the specific properties of the cotton fiber. Both cotton breeders and biotechnologists use this knowledge to explore possible modifications in key parts of the biochemical processes, which could lead to improvements in cotton fiber quality. Additionally, it was found that fiber quality and yield could be improved through transgenic approaches by over-expressing specific proteins in the fiber cell lumen or by regulating endogenous genes to enhance cell wall synthesis, elongation and deposition of cellulose.

Cotton fiber is a single elongated cell derived from the ovule epidermis. The development of cotton fiber follows a well-defined sequence of processes such as, initiation, elongation, secondary cell wall synthesis and maturation. Studies have shown that phytohormones (auxin, gibberellins, cytokinins and ethylene) play important roles in fiber development. Auxin and cytokinin are determinants of fiber initiation and the number of fibers on each seed. Exogenous application of Indole acetic acid (Auxin) on squares and flowers of cotton resulted in a significant improvement in the fiber number per ovule (Seagull *et al.*, 2004). Zhang *et al.*, (2011) reported that more than 15% increase in lint yield was possible by targeted expression of the IAA biosynthetic gene *iaaM*, driven by the promoter of the petunia MADS box gene Floral Binding protein 7 (FBP7) which is known to be active between -2 to 10 DPA (Days Post Anthesis). The targeted regulation of growth regulators such as Auxin and cytokinin in specific parts of the flowers and ovules can improve quality and yield.

Regulation of fiber specific genes of cotton- *E6, Fb-B6, Fb- B8, FbL2A* and *H6* through over-expression or gene silencing to alter the sequence of fiber development caused limited effects on fiber quality and yield since these proteins were found to be required at very low levels for normal fiber development. Genes specifically implicated in secondary wall formation of cotton fiber viz., *cesA-4, cesA-7* and *cesA-8* genes have been explored to improve fiber quality. A few other candidate genes such as Sucrose phosphate synthase *susA1* genes, *extension*, *Myb, aquaporin, expansin, annexin* have also been tried with fiber specific promoters using low fiber length and strength genotypes to improve fiber strength. Jiang, *et al.* (2012) showed that over-expression of a sucrose synthase gene *GhSusA1* increased plant biomass and improved cotton fiber yield and quality. Over-expression of these improved fiber length and strength only to a limited extent. Al-Ghazi *et al.*, (2009) found a correlation between expression of a *pectin methylesterase* gene and fiber quality. Recent studies (Hinchliffe *et al.*, 2010, 2011) showed that genes such as cellulose synthase2 (*GhCesA2*) and chitinase-like1 (*Ghctl1*) from *G. hirsutum*, and *G. hirsutum* orthologs of the Arabidopsis genes such as irregular *xylem3/cellulose synthase7* (Ghirx3), *and COBRA-LIKE4 (GhCOBL4)*, were related to fiber strength. The authors hypothesized that the targeted expression of these and also other genes associated with cellulose synthesis and microtubule rearrangement, during the transition stage of fiber development may increase fiber strength. Transgenic cotton over-expressing a profilin gene **GhPFN2** that codes for actin bundling protein resulted in higher fiber bundle strength (Bao *et al.* 2011; Hinchliffe *et al.*, 2011; Haigler *et al.*, 2012)

The family of xyloglucan endo-transglycosylase/hydrolase (**XTH**) genes degrade xyloglucan irreversibly or cleave and transfer chain ends between molecules to possibly increase the plasticity of the primary wall and promote cotton fiber elongation (Cosgrove, 2005; Eklöf and Brumer, 2010). Transgenic cotton plants constitutively over-expressing *Gossypium hirsutum* **GhXTH1** gene showed a positive correlation between twofold higher XET activity and 15–20% longer fiber length. The transgenic plants had about and longer fiber compared to wild-type cotton or null segregants under greenhouse or field conditions. Therefore, the transfer of xyloglucan chain ends between molecules was predicted to be a limiting factor for cotton fiber elongation (Lee *et al.*, 2010). Similarly, down-regulated expression of **GhADF1**, encoding an actin-depolymerizing factor, had a heritable increase in fiber length (+5.6%) and thicker secondary walls (Wang *et al.*, 2009). Recently, Chen *et al.* (2012) showed evidence that the down-regulated expression of abscisic acid (ABA) and ethylene signaling pathway genes and high-level and long-term expression of positive regulators including auxin and cell wall enzyme genes for fiber cell elongation at the fiber developmental transition stage may account for superior fiber qualities. They found that genes encoding responsive to abscisic acid 1B (*Rab1B*), ACC synthase 6 (*ACS6*), NAC and Zinc finger (C3HC4-type) family transcription factors and β-1,3-glucanase, play a specific role in preventing fiber elongation or promoting secondary cell wall synthesis.

The earliest attempts to improve cotton fiber quality using recombinant DNA technology were made by using the *poly hydroxyl butyrate*, PHB genes from bacteria (John and Keller, 1996). Subsequently, several attempts are being made for improvement of fiber quality by transferring heterologous genes from bacteria, spinach, silkworm, spiders etc. Sucrose phosphate synthase was isolated from spinach and was introduced into cotton to improve fiber quality especially under stress, (Haigler et.al. 2007). The resultant cotton transgenics pushed the fiber quality to the premium range even when grown under stressful cool night conditions. A few potential candidate genes shortlisted for fiber quality improvement are, SPS gene from spinach, *acsA* and *acsB* genes of *Acetobacter xylinum*, the spider silk gene, *spindroin* and genes governing the expression of Fibroin (*H- Fib, L-Fib, P25*), Sericin (*Ser1 and Ser 2*) and Seroin in the silk worm *Bombyx mori.*

Thus regulation of genes encoding cell wall synthesis and the genes from heterologous sources are expected to be potential candidates for improving fiber quality and yield.

Improvement of Seed Nutrition Quality

During the processing of cottonseed, most of the free gossypol is converted to the less toxic bound form, presumably by binding of the protein with epsilon amino group of lysine to free gossypol. Enhancing lysine content specifically in seeds leading to the reduction of free gossypol would make cottonseed oil more competitive and also improve nutritional quality of the meal. Low gossypol seed can be possible through biotech cotton expressing cytochrome P450 *CYP6AE14* genes from cotton bollworms to be expressed specifically in cotton seeds using seed specific promoters. Sunilkumar *et al.* (2006) utilized RNA interference to inhibit the expression of the δ-cadinene synthase gene in a seed-specific manner, thereby disrupting a key step in the biosynthesis of gossypol in cotton. Compared to an average gossypol value of 10 μg/mg in wild-type seeds, seeds from RNAi lines showed values as low as 0.2μg/mg. Importantly, the levels of gossypol and related terpenoids that are derived from the same pathway were not diminished in the foliage and floral parts of mature plants and thus remain available for plant defense against insects and diseases. Apart from silencing of *δ*-cadinene synthase, there are several innovative strategies that can be used to reduce gossypol specifically in seeds and also to increase monounsaturated fatty acids to make cotton seed oil more acceptable nutritionally.

Marker Assisted Breeding

A well focused approach on identification of markers for economically important traits can assist in accelerating and improving precision in plant breeding strategies. Plant Breeders, all over the world, have so far subjected germplasm resources to intensive breeding, so as to enhance yield, fiber quality traits, high oil content or resistance to biotic or abiotic stresses. Such programs also inadvertently resulted in narrowing of the genetic base. Out of the 50 cotton species, 5 are considered to be in the primary germplasm pool, 21 as secondary and 24 as tertiary germplasm pools, based on the relative genetic accessibility.

Currently, there are published genetic maps of useful traits and markers, which include ~ 5,000 markers in public databases including 3,300 RFLP, 700 amplified frabiotechent length polymorphism (AFLP), 1,000 SSR, and 100 single nucleotide polymorphism (SNP) (Rahman *et al.*, 2011). The clarity on crucial metabolic networks responsible for fiber development is enhancing more and more with the recent advances in transcriptome data and the progress in cotton genomics. Recent transcriptomic and proteomic studies (Al-Ghazi *et al.* 2009; Rapp *et al.* 2010; Xie *et al.* 2011; Kang *et al.* 2012) reveal the mechanisms governing cotton fiber differentiation and initiation. Yu *et al.* (2012) published a high-density simple sequence repeat and single nucleotide polymorphism genetic map of the tetraploid cotton genome. Byers *et al.* (2012) developed and mapped SNP assays in allotetraploid cotton. Xiao *et al.*, (2009) identified highly informative 2,937 SSR primer pairs, which target unique genomic sequences and amplify about 4,000 unique marker loci in a tetraploid cotton genome. Chromosome-marker bins, each 20 cM in size, were constructed on the genetic linkage map containing the markers. Thus 207 marker bins were assigned for a total of about 4,140 cM, which is approximately the size of the tetraploid cotton genetic map. QTLs for fiber quality traits and yield attributes have been elucidated (An *et al.*, 2010; Lacape *et al.*, 2010; Shen *et al.*, (2011; Zhang *et al.*, 2011; Claverie *et al.*, 2012). With such a tremendous pace of improvement in the molecular aspects of fiber development, it has now become possible to link fiber QTLs to the expression of crucial genes involved in fiber development and other QTLs related to yield components with the background of transcriptomics, proteomics and metabolomics, to identify strategies for fiber quality and yield improvement through marker assisted breeding and also through transgenic approaches.

There are several examples of identification and validation of molecular markers that have been tightly linked to economically important traits in cotton. Genomics of drought tolerance has unraveled new insights into the plant responses to abiotic stress (Saranga *et al.*, 2004; Zhao *et al.*, 2008; Ullah 2009). Markers linked with cotton resistance to Verticillium (Wang *et al.*, 2008) and cotton leaf curl disease (Rahman *et al.*, 2006) are also being studies intensively for use in Marker assisted breeding. Shen *et al.* (2010) showed that the dominant factor Mi1 linked to root knot nematode in cotton resistance is located on chromosome 11. The Mi-C11 locus was delimited to a 3.6-cM interval flanked by the SSR marker CIR069 and the AFLP marker E14M27-375. Dighe *et al.*, 2009 mapped an allele Ren^{lon} on chromosome 11 for extreme resistance for reniform nematode that was introgressed from the African species *G. longicalyx*. In a recent outstanding example of mapping SNP/SSR markers to an economically important trait, Xiao *et al.* (2010) found that three markers CIR 246, BNL 3545 and BNL 3644 on chromosome 14, were found closely linked to B_{12} gene which is a major gene contributing maximum bacterial blight resistance to almost all the races of Xanthomonas axonopodis malvacearum Xam. One of the SNP/SSR markers, was closely linked (3.4 cM) to resistance gene B_{12} on chromosome 14 and can be used for validation in mapping populations to be utilized in marker assisted breeding programs. These markers can be used effectively to tag quantitative traits of interest in the already characterized germplasm pools and thereafter utilize in marker assisted breeding programs for genetic enhancement of elite lines and genotypes to develop multi-stress-resistant high yielding high quality fiber cultivars.

Upstream biotechnology in cotton presents exciting prospects. The science of genomics has moved rapidly with the availability D-genome sequences and a wide range of annotated markers. The advances have set the stage for cotton breeding by design to selectively incorporate economically desirable traits into elite varieties through marker assisted breeding avoiding undesirable linkage drag. A wide array of novel genes are available for use in genetic transformation systems to develop cotton varieties with superior fiber quality, wider adaptability, resistance to drought, water-logging, salinity, heat, insect pests, pathogens and nematodes. The progress in cotton biotechnology is seen as an outstanding example of successful application of biotechnology for problem solving and product quality enhancement in Agricultural sciences that holds tremendous promise for today and the future.

Literature

Addison, S., Farrell, T., Roberts, G. and Rogers, D. (2007). Roadside surveys support predictions of negligible naturalisation potential for cotton in north-east Australia. *Weed Research* 47, 192-201.

Al-Ghazi, Y., Bourot, S., Arioli, T., Dennis, E.S. and Llewellyn, D.J. (2009). Transcript profiling during fiber development identifies pathways in secondary metabolism and cell wall structure that may contribute to cotton fiber quality. *Plant Cell Physiol 50*: 1364–1381

An, Chuanfu, Johnie, N. Jenkins, Jixiang Wu, Yufang Guo and Jack C. McCarty. (2010). Use of fiber and fuzz mutants to detect QTL for yield components, seed, and fiber traits of upland cotton. *Euphytica* 172; 21–34.

Arora, A. and Bansal, S. (2010). Diffusion of Bt cotton in India: Impact of seed prices and technological development (Unpublished technical paper). New Delhi, India: Jawaharlal Nehru University, Centre for International Trade and Development, School of International Studies.

Bange, M.P., Caton, S.J. and Milroy, S.P. (2008). Managing yields of high fruit retention in transgenic cotton (*Gossypium hirsutum* L.) using sowing date. *Australian Journal of Agricultural Research* 59: 733-741.

Barry, G.F., Kishore, G.M., Padgette, S.R. and Stallings, W.C. (1997), Glyphosate-tolerant 5-enolpyruvylshikimate-3-phosphate synthases. U.S. Patent 5633435.

Bao, Y., Guanjing Hu, Lex E. Flagel, Armel Salmon, Magdalena Bezanilla, Andrew H. Paterson, Zining Wang and Jonathan F. Wendel. (2011). Parallel up-regulation of the profilin gene family following independent domestication of diploid and allopolyploid cotton (Gossypium). *Proc. Natl. Acad. Sci. USA*, 108; 21152-21157.

Beale, Michael H., Michael A. Birkett, Toby J. A. Bruce, Keith Chamberlain, Linda M. Field, Alison K. Huttly, Janet L. Martin, Rachel Parker, Andrew L. Phillips, John A. Pickett, Ian M. Prosser, Peter R. Shewry, Lesley E. Smart, Lester J. Wadhams, Christine M. Woodcock, and Yuhua Zhang. (2006). Aphid alarm pheromone produced by transgenic plants affects aphid and parasitoid behavior. *Proc. Natl. Acad. Sci. USA*, 103; 10509-10513.

Becker, Geoffrey S. and Charles Hanrahan. (2003). *U.S. Agricultural Biotechnology in Global Markets: An Introduction*. CRS Report for Congress, Order Code RL31970.

Bergé, J,B. and Ricroch, A,E. (2010). Emergence of minor pests becoming major pests in GE cotton in China. *GM Crops* 1(4): 214-219

Bird, L.S. (1982). The MAR (multi-adversity-resistance) system for genetic improvement of cotton. *Plant Disease*. 66, 172-176.

Bolek, Y., El-Zik, K.M., Pepper, A.E., Bell, A.A., Magill, C.W., Thaxton, P.M., Reddy, O.U.K. (2005). Mapping of verticillium wilt resistance genes in cotton. *Plant Sci*. 168, 1581-1590.

Brodrick, R., Bange, M.P., Milroy, S.P. and Hammer, G.L. (2010). Yield and maturity of ultra-narrow row cotton in high input production systems. *Agronomy Journal* 103, 843-848.

Brown, A.H.D., Brubaker, C.L. and Kilby, M.J. (1997). Assessing the risk of cotton transgene escape into wild Australian *Gossypium* species. *In* GD McLean, PM Waterhouse, G Evans, MJ Gibbs, eds. *Commercialisation of transgenic crops: risk, benefit and trade considerations*. Bureau of Resource Sciences, Canberra. pp 83-93.

Brookes, Graham and Peter Barfoot. (2011). The income and production effects of biotech crops globally 1996-2009. *International J. Biotech*. 12:1-49.

Brookes, Graham. (2012). Economic impacts of the Biosafety Law and implementing regulations in Turkey on the Turkish importing and user sectors. PG Economics Ltd., UK. http://www.biotecho-compass.org/pdf/documents/TurkeybiosafetylawimpactfinalreportPGEconomicsMay2012.pdf

Burgos, N,, Culpepper, S., Dotray, P., Kendig, A., Wilcut, J. and Nichols, R. Managing Herbicide Resistance in Cotton Cropping Systems. Available at http://www.cotton.org/tech/pest/upload/07CIweedresistbulletin.pdf

Byers, R.L., Harker, D.B., Yourstone, S.M., Maughan, P.J. and Udall, J.A. (2012). Development and mapping of SNP assays in allotetraploid cotton. *Theor Appl Genet.*, 124; 1201–1214.

Calestous Juma. June 23, 2011a. *Agricultural Biotechnology: Benefits, Opportunities, and Leadership*. Testimony to the U.S. House of Representatives, Committee on Agriculture, Subcommittee on Rural Development, Research, Biotechnology, and Foreign Agriculture.

Carriere, Y., Ellers-Kirk, C., Sisterson, M., Antilla, L., Whitlow, M., Dennehy, T.J. and Tabashnik, B.E.. (2003). Long-term regional suppression of pink bollworm by Bacillus thuringiensis cotton. *Proc Natl Acad Sci*, USA 100: 1519–1523.

Cattaneo, M. G., Yafuso, C., Schmidt, C., Huang, C., Rahman, M., Olson, C., Ellers-Kirk, C., Orr, B., Marsh, S.E., Antilla, L., Dutilleul, P., and Carrière, P. (2006). Farm-scale evaluation of the impacts of transgenic cotton on biodiversity, pesticide use, and yield. Proc. Natl Acad. Sci. USA 103, 7571–7576.

Candace H., Yafuso, C., Schmidt, C., Huang, C., Rahman, M., Olson, C., Ellers-Kirk, C., Orr, B.J., Marsh, S.E., Antilla, L., Dutilleul, P. and Carrière, Y. (2012). Cotton fiber: a powerful single-cell model for cell wall and cellulose research. *Front Plant Sci.*, 3; 104

Chen, X., Guo, W., Liu, B., Zhang, Y., Song, X., Cheng, Y., Zhang, L. and Zhang, T. (2012). Molecular Mechanisms of Fiber Differential Development between *G. barbadense* and *G. hirsutum* Revealed by Genetical Genomics. *PLoS ONE*, 7(1): e30056 doi:10.1371/journal.pone.0030056.

Charles, G.W. and Taylor, I.N. (2003). Herbicide resistance and species shift in cotton: The need for an integrated weed management (IWM) approach. *Proceedings of the World Cotton Research Conference-3*. Cape Town, South Africa, March 2003.

Charles, G.W., Constable, G.A. and Kennedy, I.R. (1995). Current and future weed control practices in cotton: the potential use of transgenic herbicide resistance. *In* Herbicide-resistant crops and pastures in Australian farming systems. Proceedings of a workshop held in Canberra, March 15-16, 1995. Ed GD McLean and G Evans. Department of Primary Industry and Energy; Bureau of Resource Sciences.

Claverie, M., Souquet, M., Jean, J., Forestier-Chiron, N., Lepitre, V., Pré, M., Jacobs, J., Llewellyn, D. and Lacape, J.M. (2012). cDNA-AFLP based genetical genomics in cotton fibers. *Theor Appl Genet* ,124; 665–683.

Constable, G.A., Thomson, N.J. and Reid, P.E. (2001). Approaches utilized in breeding and development of cotton cultivars in Australia. *In* Genetic Improvement of Cotton: Emerging Technologies. J.N. Jenkins and S. Saha (Eds). Science Publishers, Enfield. pp 1-15.

Constable, G.A., Reid, P.E. and Stiller, W.N. (2007). Breeding for resistance to a new strain of Fusarium wilt in Australia. *Proceedings of the World Cotton Research Conference-4*. Lubbock, USA, Sept 2007. http://wcrc.confex.com/wcrc/2007/techprogram/P1689.HTM.

Cosgrove, D. J. (2005). Growth of the plant cell wall. *Nat Rev Mol Cell Biol* 6:850–861

De Barro, P.J., Liu, S-S., Boykin, L.M. and Dinsdale, A.B. (2011). ***Bemisia tabaci***: A statement of species status. *Annual Review of Entomology* 56, 1-19.

Dennis, E.S., Ellis, J., Green, A., Llewellyn, D., Morell, M., Tabe, L. and Peacock, W.J. (2008). Genetic contributions to agricultural sustainability. *Philosophical Transactions of the Royal Society B* 363, 591-609.

Dighe, N.D., Robinson, A.F., Bell, A.A., Menz, M.A., Cantrell, R.G. and Stelly, D.M. (2009). Linkage Mapping of Resistance to Reniform Nematode in Cotton following Introgression from *Gossypium longicalyx* (Hutch. & Lee). *Crop Science,* 49;1151-1164.

Dhurua, S. and Gujar, G.T. (2011). Field-evolved resistance to Bt toxin Cry1Ac in the pink bollworm, *Pectinophora gossypiella* (Saunders) (Lepidoptera: Gelechiidae), from India. *Pest Manag Sci* 67: 898–903.

Downes, S.J., Mahon, R. and Olsen, K. (2007). Monitoring and adaptive resistance management in Australia for Bt-cotton: Current status and future challenges. *Journal of Invertebrate Pathology* 95, 208-213.

Downes, S.J. and Mahon, R. (2012a). Successes and challenges of managing resistance in Helicoverpa armigera to Bt cotton in Australia. *In* BIOTECH Crops & Food: Biotechnology in Agriculture and the Food Chain Volume 3 Issue 3, July/August/September, http://www.landesbioscience.com/journals/36/article/20194/

Downes, S.J. and Mahon, R. (2012b). Evolution, ecology and management of resistance in *Helicoverpa* spp. to Bt cotton in Australia. *Journal of Invertebrate Pathology* 110, 281-286.

Downes, S.J., Parker, T. and Mahon, R. (2010). Incipient resistance of *Helicoverpa punctigera* to the Cry2Ab Bt toxin in Bollgard II® cotton. *PLoS ONE* 5, e12567.

Eastick, R. and Hearnden, M. (2006). Potential for weediness of Bt-cotton in Northern Australia. *Weed Science* 54, 1142-1151.

Eklöf J.M. and Brumer, H. (2010). The *XTH* Gene Family: An Update on Enzyme Structure, Function, and Phylogeny in Xyloglucan Remodeling. *Plant Physiology*, 153; 2 456-466.

European Food Safety Authority; Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphosate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. *EFSA Journal* 2012; 10(10): 2910-2919

Farrell, T. and Roberts, G. (2002). Survey of cotton volunteers north of latitude 22° south. Australian Cotton CRC and CSIRO Plant Industry, Narrabri, Australia

Faircloth, W.H., Patterson, M.G., Monks, C.D. and Goodman, W.R. (2001). Weed Management Programs for Glyphosate-Tolerant Cotton (Gossypium hirsutum). *Weed Technology* 26(3): 544-551.

Fitt, G.P. (1994). Cotton pest management: Part 3 - an Australian perspective. *Annual Review of Entomology* 39, 543-562.

Fitt, G.P. (2000). An Australian approach to IPM in cotton: integrating new technologies to minimise insecticide dependence. *Crop Protection* 19, 793-800.

Fitt, G.P. and Cotter, S. 2004. Chapter 4. The *Helicoverpa* problem in Australia. *In* Sharma H. (ed). *Heliothis*/*Helicoverpa* Management: Emerging Trends and Strategies for Future Research. Oxford and IBH Publishing, New Delhi. Pp. 45-62.

Fitt, G.P. and Daly, J.C. (1990). Abundance of overwintering pupae and the spring generation of *Helicoverpa* spp. (Lepidoptera: Noctuidae) in northern New South Wales, Australia: implications for pest management. *Journal of Economic Entomology* 83, 1827-1836.

Fitt, G.P., Mares, C.L. and Llewellyn, D.J. (1994). Field evaluation and potential ecological impact of transgenic cottons (*Gossypium hirsutum*) in Australia. *Biocontrol Science and Technology* 4, 535-548.

Forrester, N.W., Cahill, M., Bird, L.J. and Layland, J.K. (1993). Management of pyrethroid and endosulfan resistance in *Helicoverpa armigera* (Lepidoptera: Noctuidae) in Australia. *Bull Ent Res Supplement Series, Supplement No 1*. 132 pp.

Fournier, A., Ellsworth, P.C. and Barkley, V.M. (2007). Economic Impact of Lygus in Arizona Cotton: A Comparative Approach. Arizona Cotton Report P-151: 155-166

Gruere, Guillaume P. Asynchronous Approvals of GM Products, Price Inflation, and the Codex Annex: What Low Level Presence Policy for APEC Countries? Paper presented at the International Agricultural Trade Research Consortium Analytic Symposium "Confronting Food Price Inflation: Implications for Agricultural Trade and Policies", June 22-23, 2009, Seattle, Washington.

Gunning, R.V., Byrne, F.J., Conde, B.D., Connelly, M.I., Hergstrom, K. and Devonshire, A.L. (1995). First report of B biotype *Bemisia tabaci* (Gennadius) (Hemiptera: Aleyrodidae) in Australia. *J Aust Entomol Soc* 34,116.

Gunning R.V., Moores G.D. and Devonshire, A.L. (1996). Insensitive acetylcholinesterase and resistance to Thiodicarb in Australian *Helicoverpa armigera* Hübner (Lepidoptera: Noctuidae) *Pestic Biochem Physiol.* 55, 21–28.

Haigler, C.H., Singh, B., Zhang, D., Hwang, S., Wu, C., Cai, W.X., Hozain, M., Kang, W., Kiedaisch, B., Strauss, R.E., Hequet, E., Wyatt, B.W., Jviden, G.M. and Holaday, A.S. (2007). Transgenic cotton over-producing spinach sucrose phosphate synthase showed enhanced leaf sucrose synthesis and improved fiber quality under controlled environmental conditions*. Plant Mol Biol*, 63;815–832

Herron, G.A., Edge, V., Wilson, L. J. and Rophail, J. (1998). Organophosphate resistance in spider mites (Tetranychidae) from cotton in Australia. *Exp. Appl. Acarol.* 22, 17-30.

Herron, G.A., Powis, K. and Rophail, J. (2001). Insecticide resistance in *Aphis gossypii* Glover (Hemiptera: Aphididae), a serious threat to Australian cotton. *Aust. J. Entomol.* 40, 85-89.

Herron, G.A., Rophail, J. and Wilson, L.J. (2001). The evolution of bifenthrin resistance in two-spotted spider mite (Acari: Tetranychidae) from Australian cotton. *Exp. Appl. Acarol.* 25, 301-310.

Herron, G.A., Rophail, J. and Wilson, L.J. (2004). Chlorfenapyr resistance in two-spotted spider mite (Acari: Tetranychidae) from Australian cotton. *Exp. Appl. Acarol.* 34, 315-321.

Hillocks, R.J. (1992). *Cotton Diseases*. Ed RJ Hillocks, CABI; UK. 415 pp.

Hinchliffe, D.J., Meredith, W.R., Yeater, K.M., Kim, H.J., Woodward, A.W., Chen, Z.J. and Triplett, B.A. (2010). Near-isogenic cotton germplasm lines that differ in fiber-bundle strength have temporal differences in fiber gene expression patterns as revealed by comparative high-throughput profiling. *Theor. Appl. Genet.*, 120; 1347–1366.

Hinchliffe, D.J., Meredith Jr, W.R., Delhom, C.D., Thibodeaux, D.P. and Fang, D.D. (2011). Elevated growing degree days influence transition stage timing during cotton fiber development resulting in increased fiber-bundle strength. *Crop Sci.*, 51; 1683–1692.

Hozain, M., Abdelmageed, H., Lee, J., Kang, M., Fokar, M., Allen, R.D. and Holaday, A.S. (2012). Expression of AtSAP5 in cotton up-regulates putative stress-responsive genes and improves the tolerance to rapidly developing water deficit and moderate heat stress. *Journal of Plant Physiology*, 169; 1261–1270.

James, Clive. (2011). Global Status of Commercialized Biotech/GM Crops: 2011. ISAAA Brief No. 43. ISAAA: Ithaca, NY.

James, C. (2012). Global Status of Commercialized Biotech/GM Crops: 2012, ISAAA Brief No. 44, ISAAA: Ithaca, NY.

Jiang, Y.P., Cheng, F., Zhou, Y.H., Xia, X.J., Mao, W.H., Shi, K., Chen, Z.X. and Yu. J.Q. (2012). Hydrogen peroxide functions as a secondary messenger for brassinosteroids-induced CO(2) assimilation and carbohydrate metabolism in *Cucumis sativus*. *J Zhejiang Univ Sci B.*, 13; 811-23.

John, M.E. (1999). Genetic engineering strategies of cotton fiber modification. in CottonFibers: *Developmental Biology, Quality Improvement and Textile Processing* (ed. Basra, A.S.). 271–292 (The Haworth Press, New York, USA).

John, M.E. and Keller, G. (1996). Metabolic pathway engineering in cotton: Biosynthesis of polyhydroxybutyrate in fiber cells. *Proc. Natl. Acad. Sci.*, 93; 12768–12773.

Kalaitzandonakes, Nicholas. (2011). The Economic Impacts of Asynchronous Authorizations and Low Level Presence: An Overview. International Food & Agricultural Trade Policy Council.

Khadi, B.M. Biotech Cotton: Issues for Consideration. ICAC (available in https://www.icac.org/tis/regional_networks/documents/asian/papers/khadi.pdf)

Kennedy, I., Crossan, A., Burns, M. and Shi, Y. (2011), Fate and transport of agrochemicals in the environment. *In* **Kirk Othmer Encyclopedia of Chemical Technology,** Arza Seidel, Ed.**,** John Wiley & Sons, In press (accepted Jan 18, 2011).

Knox, O.G., Constable, G.A., Pyke, B. and Gupta, V.V.S.R. (2006). Environmental impact of .conventional and Bt insecticidal cotton expressing one and two Cry genes in Australia. *Australian Journal of Agricultural Research* 57, 501-9.

Kochman, J.K. (1995). Fusarium wilt in cotton – a new record in Australia. *Australasian Plant Pathology* 24, 74.

Lacape, J.M. (2010). Meta-analysis of cotton fiber quality QTLs across diverse environments in a *Gossypium hirsutum* × *G. barbadense* RIL population. *BMC Plant Biol*, 10;132

Lacape, J.M., Nguyen, T.B., Courtois, B., Belot, J-L., Giband, M., Gourlot, J-P., Gawryziak, G, Roques, S. and Hau, B. (2005). QTL analysis of cotton fiber quality using multiple *Gossypium hirsutum x Gossypium barbadense* backcross generations. *Crop Sci.* 45, 123-140.

Lagos, Joshua Emmanuel and Wu Bugang. (2011). People's Republic of China, Biotechnology – GE Plants and Animals. GAIN Report No. CH11002.

Lee J., Burns, T.H., Light, G., Sun, Y., Fokar, M., Kasukabe, Y., Fujisawa, K., Maekawa, Y. and Allen, R.D. (2010). Xyloglucan endotransglycosylase/hydrolase genes in cotton and their role in fiber elongation. *Planta*, 232; 1191–1205.

Leemans, J., Botterman, J., de Block, M., Thompson, C. and Mouva, R. (1992). Plant cells resistant to glutamine synthetase inhibitors, made by genetic engineering. Patent EP 0242246 B1.

Li, H.B., Wu, K.M., Xu, Y., Yang, X.R., Yao, J. and Wang, F. (2007). Population dynamics of pest mirids in cotton field in Southern Xinjiang. Chinese Bull. *Entomology* 44:219-22.

Llewellyn, D.J. and Fitt, G. (1996). Pollen dispersal from two field trials of transgenic cotton in the Namoi valley, Australia. *Molecular Breeding* 2, 157-166.

Llewellyn, D.J., Tyson, C., Constable, G.A., Duggan, B., Beale, S. and Steel, P. (2007). Containment of regulated genetically modified cotton in the field. *Agriculture, Ecosystems & Environment* 121: 419-429.

Lusser, Maria, Terri Raney, Pascal Tillie, Koen Dillen and Emilio Rodriguez Cerezo. (2012). International workshop on socio-economic impacts of genetically modified crops co-organised by JRC-IPTS and FAO. JRC Scientific and Policy Reports.

Lu Y.H., Wu, K., Jiang, Y., Xia, B., Li, P., Feng, P., Wyckhuys, K.A.G. and Guo, Y. (2010). Mirid bug outbreaks in multiple crops correlated with wide-scale adoption of Bt cotton in China. *Science* 328, 1151–1154.

Lu, Y. H., K. M. Wu, Y. Y. Jiang, Y. Y. Guo, and N. Desneux. 2012. Widespread adoption of Bt cotton and insecticide decrease promotes biocontrol services. *Nature* 487: 362–365

Lu, B., Downes, S.J., Wilson, L., Gregg, P., Knight, K., Kauter, G. and McCorkell, B. (2012a). Yield, development and quality response of dual-toxin Bt cotton to *Helicoverpa* spp. infestations in Australia. *Agriculture, Ecosystems and Environment* (In press).

Lu, B., Downes, S.J., Wilson, L., Gregg, P., Knight, K., Kauter, G. and McCorkell, B. (2012b). Yield, development and quality response of dual-toxin Bt cotton to manual simulation of damage by *Helicoverpa* spp. in Australia. *Crop Protection* (In press).

Mahon, R., Olsen, K., Downes, S.J. and Addison, S. (2007). Frequency of alleles conferring resistance to the Bt toxins Cry1Ac and Cry2Ab in Australian populations of *Helicoverpa armigera* (Hübner) (Lepidoptera: Noctuidae). *Journal of Economic Entomology* 100, 1844-1853.

Mahon, R., Downes, S.J. and James, W. (2012). Vip3A resistance alleles exist at high levels in targets before release of cotton expressing this toxin. *PLoS ONE* 7(6), e39192.

Main C.L., Jones, M.A. and Murdock, E.C. (2007). Weed Response and Tolerance of Enhanced Glyphosate-Resistant Cotton to Glyphosate. *The Journal of Cotton Science* 11:104–109.

Mal, P., Manjunatha, A.V., Bauer, S. and Ahmed, M.N. (2011). Technical efficiency and environmental impact of Bt cotton and non-Bt cotton in North India. *AgBioForum*, 14(3), 164-170.

Mansfield, S. Dillon, M.L. and Whitehouse, M.E.A. (2006). Are arthropod communities in cotton really disrupted? An assessment of insecticide regimes and evaluation of the beneficial disruption index. *Agriculture, Ecosystems and Environment* 113, 326-335.

Mao, Y.B., Cai, W.J., Wang, J.W., Hong, G.J., Tao, X.Y., Wang, L.J., Huang, Y.P. and Chen, X.Y. (2007). Silencing a cotton bollworm P450 monooxygenase gene by plant-mediated RNAi impairs larval tolerance of gossypol. *Nature Biotechnology*, 25; 1307–1313.

Marvier, M., McCreedy, C., Regetz, J. and Kareiva, P. (2007). A meta-analysis of effects of Bt cotton and maize on nontarget invertebrates. *Science* 316, 1475-1477.

May, O.L. (1999). Genetic variation in fiber quality. pp 183-229. *In* A.S. Basra (ed) Cotton Fibers. Food Products Press, New York.

May, O.L. and Taylor, R.A. (1998). Breeding cottons with higher yarn tenacity. *Textile Research Journal* 68, 302-307.

May, O.L., Bourland, F.M. and Nichols, R.L. (2003). Challenges in testing transgenic and non-transgenic cotton cultivars. *Crop Science* 43, 1594-1601.

May, O.L., Culpepper, A.S., Cerny, R.E., Coots, C.B., Corkern, C.B., Cothren, J.T., Croon, K.A., Ferreira, K.L., Hart, J.L., Hayes, R.M., Huber, S.A., Martens, A.B., McCloskey, W.B., Oppenhuizen, M.E., Patterson, M.G., Reynolds, D.B., Shappley, Z.W., Subramani, J., Witten, T.K., York, A.C. and Mullinix, B.G. (2004). **Transgenic cotton with improved resistance to glyphosate herbicide.** *Crop Science* 44, 234-240.

Mawhinney, W. (2011). Namoi water quality project 2002-2007 final report. New South Wales Office of Water. 41pp. ISBN 0-7347-5771-9. *In press*. (www.water.nsw.gov.au)

Nandula, V.K., Reddy, K.N., Duke, S.O. and Poston, D.H. (2005). Glyphosate-resistant weeds: current status and future outlook. *Outlooks on Pest Management* 16:183-187

Naranjo, S.E., Ellsworth, P.C. (2010). Fourteen years of Bt cotton advances IPM in Arizona. *Southwestern Entomol* 35: 437–444.

Naranjo, S.E., Ruberson, J.R., Sharma, H.C., Wilson, L.J. and Wu, K. (2008). The present and future role of insect-resistant BIOTECH crops in cotton IPM. *In* Integration of Insect-resistant BIOTECH crops within IPM Programs. Edited by J. Romeis, A. M. Shelton, and G. G. Kennedy. Springer Science and Business Media BV, pp 158-194.

National Research Council. (2010). The impact of genetically engineered crops on farm sustainability in the United States. National Academies Press.

Park, W., Scheffler, B.E., Bauer, P.J. and Campbell, B.T. (2012). Genome-wide identification of differentially expressed genes under water deficit stress in upland cotton (*Gossypium hirsutum* L.). *BMC Plant Biology*, 12; 90.

Park, Y-H., Alabady, M.S., Ulloa, M., Sickler, B., Wilkins, T.A., Yu, J., Stelly, D.M., Kohel, R.J., Shihy, O.M.I. and Cantrell, R.G. (2005) Genetic mapping of new cotton fiber loci using EST-derived microsatellites in an interspecific recombinant inbred line cotton population. *Molecular Genetics and Genomics* 274, 428-441.

Powles, S.B. (2008). Evolved glyphosate-resistant weeds around the world: lessons to be learnt. *Pest Management Science* 64, 360–365.

Pray, E.C. and Nagarajan, L. (2010). Price Controls and Biotechnology Innovation: Are State Government Policies Reducing Research and Innovation by the Ag Biotech Industry in India? AgBioForum, 13(4) Article 2

Qaim, M. and Basu, A.K. (2007). On the Adoption of genetically modified seeds in developing countries and optimal types of government intervention. *American Journal of Agricultural Economics* 89(3): 784-804.

Rahman, M., Hussain, D., Malik, T.A. and Zafar, Y. (2005). Genetics of resistance against cotton leaf curl disease in *Gossypium hirsutum*. *Plant Pathol*, 54; 764-772.

Rapp R.A., Candace, H. Haigler, Lex Flagel, Ran H. Hovav, Joshua A. Udall and Jonathan F. Wendel. (2010). Gene expression in developing fibres of Upland cotton (*Gossypium hirsutum*L.) was massively altered by domestication *BMC Biology*, 8; 139.

Reddall, A., Ali, A. and Able, J. (2004). Cotton bunchy top (CBT): an aphid and graft transmitted cotton disease. *Australasian Plant Pathology* 33, 197-202.

Rodriguez-Uribea L., Higbie, S.M., Stewart, J.M., Wilkins, T., Lindemann, W., Sengupta-Gopalan C. and Zhang, J. (2011). Identification of salt responsive genes using comparative microarray analysis in Upland cotton (Gossypium hirsutum L.) *Plant Sci.*, 180; 461-469.

Rossiter, L., Gunning, R. and McKenzie, F. (2008). Silver anniversary of resistance management in the Australian cotton industry. An overview and the current situation for *Helicoverpa armigera. Proceedings of the 2008 Australian Cotton Conference*, Broadbeach, August 2008.

Sadashivappa, P. and Matin Qaim. 2009. Bt cotton in India: Development of benefits and the role of government seed price interventions. *AgBioForum* 12(2): 172-183.

Saigo, Holly. 2000. Agricultural Biotechnology and the Negotiation of the Biosafety Protocol. *Georgetown International Environmental Law Review* Vol. 12:779-816.

Saranga, Y., C-X. Jiang, R.I. Wright, D. Yakir and A.H. Paterson. (2004). Genetic dissection of cotton physiological responses to arid conditions and their inter-relationships with productivity. *Plant, Cell & Environment*, 27; 263–277.

Seagull R.W. and Sofia Giavalis. (2004). Pre- and Post- Anthesis Application of Exogenous Hormones Alters Fiber Production in *Gossypium hirsutum* L. Cultivar Maxxa GTO. *The Journal of Cotton Science*, 8; 105–111

Séralini G.E., et al. (2012). Two-year rodent feeding study with glyphosate formulations and GM maize NK603, *EFSA Journal*, 10; 2910-2919

Séralini, G, E. Emilie Claira, Robin Mesnagea, Steeve Gressa, Nicolas Defargea, Manuela Malatestab, Didier Hennequinc and Joël Spiroux de Vendômoisa. (2012). Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food and Chemical Toxicology, http://dx.doi.org/10.1016/j.fct.2012.08.005

Sequeira, R.V. and Naranjo, S.E. (2008). Sampling and management of *Bemisia tabaci* (Genn.) biotype B in Australian cotton. *Crop Protection* 27, 1262-1268.

Shelton, A. M., Zhao, J. Z. and Roush, R. T. Economic, ecological, food safety and social consequences of the deployment of Bt transgenic plants. *Annu. Rev. Entomol*. 47, 845–881 (2002).

Segarra, Alejandro E. and Susan R. Fletcher. (2001). Biosafety Protocol for Genetically Modified Organisms: Overview. Report for Congress Order Code RL30594.

Sheldon, Ian M. (2001). Regulation of biotechnology: Will we ever "freely" trade GMOs? 77th EAAE Seminar/NJF Seminar No. 325, August 17-18, 2001, Helsinki.

Shen, X., He, Y., Lubbers, E.L., Davis, R.F., Nichols R.L. and Chee, P.W. (2010). Fine mapping *QMi-C11* a major QTL controlling root-knot nematodes resistance in Upland cotton. *Theoretical and Applied Genetics.*, 121; 1623-1631.

Shen, X., Cao, Z., Singh, R., Lubbers, E.L., Xu, P., Smith, C.W., Paterson, A.H. and Chee, P.W. (2011). Efficacy of qFL-chr1, a quantitative trait locus for 52 fiber length in cotton (Gossypium spp.). *Crop Sci.,* 51; 2005–2010.

Stewart, J.McD. (1995). Potential for crop improvement with exotic germplasm and genetic engineering. *In* Challenging the future: *Proceedings of the World Cotton Research Conference-1*, Brisbane Australia, February 14-17, ACCRA, pp. 313-327.

Stiller, W., Reid, P. and. Constable. G. (2006). Lessons learnt in developing transgenic cotton (*Gossypium hirsutum*) varieties. *In* C. F. Mercer, (ed.) *Proceedings of the13th Australasian Plant Breeding Conference*, Christchurch, NZ.

Sunilkumar G., LeAnne M. Campbell, Lorraine Puckhaber, Robert D. Stipanovic, and Keerti S. Rathore. (2006). Engineering cottonseed for use in human nutrition by tissue specific reduction of toxic gossypol. *Proc Natl Acad Sci USA*, 103;18054-9.

Stein, Alexander J. and Emilio Rodríguez-Cerezo. 2010a. *The global pipeline of new BIOTECH crops: Implications of asynchronous approval for international trade*. European Commission, Joint Research Centre, Institute for Prospective Technological Studies.

Stein, Alexander J. and Rodríguez-Cerezo, Emilio. (2010b). Low-Level Presence of New BIOTECH Crops: An Issue on the Rise for Countries Where They Lack Approval. AgBioForum, Vol. 13, No. 2, Article 8.

Tann, C., Fitt, G. and Baker, G. (2002). Selecting the right refuges for Bt cotton. *The Australian Cottongrower* 23:8-11

Timbs, S., Adams, K. and Rogers, W.M. (2006). Statutory review of the Gene Technology Act 2000 and the Gene Technology Agreement. Available on-line http://www.health.gov.au/internet/main/publishing.nsf/Content/gene-gtmc.htm, Commonwealth of Australia. ISBN: 0 642 82908 X. pp85-92.

Ullah, I. (2009). Molecular Genetic Studies for Drought Tolerance in Cotton. Ph.D. thesis, Quaid-i-Azam University, Islamabad, Pakistan

Verhalen, L.M., Greenhagen, B.E. and Thacker, R.W. (2003). Lint yield, lint percentage and fiber quality response in Bollgard, Roundup Ready and Bollgard/Roundup Ready cotton. *Journal of Cotton Science* 7, 23-38.

Wan, P., Huang, Y., Tabashnik, B.E., Huang, M. and Wu, K. (2012). The Halo Effect: Suppression of Pink Bollworm on Non-Bt Cotton by Bt Cotton in China. PLoS ONE 7(7): e42004. doi:10.1371/journal.pone.0042004

Wan, P., Huang, Y., Wu, H., Huang, M., Cong, S., Tabashnik, B.E. and Wu, K. (2012). Increased Frequency of Pink Bollworm Resistance to Bt Toxin Cry1Ac in China. http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0029975

Wan, P., Wu, K., Huang, M. and Wu, J. (2004). Seasonal pattern of infestation by pink bollworm Pectinophora gossypiella (Saunders) in field plots of Bt transgenic cotton in the Yangtze River Valley of China. *Crop Prot* 23: 463–67.

Wang, H-M., Lin, Z-X., Zhang, L., Chen, W., Guo, X-P., Nie, Y-C and Li, Y-H. (2008). Mapping and Quantitative Trait Loci Analysis of Verticillium Wilt Resistance Genes in Cotton. *Journal of Integrative Plant Biology*, 50; 174–182.

Wang H., Wang, J., Gao, P., Jiao, G.L., Zhao, P.M., Li, Y., Wang, G.L. and Xia GX (2009). Down-regulation of GhADF1 gene expression affects cotton fibre properties. *Plant Biotechnol. J.*, 7; 13–23.

Werth, J.A., Preston, C., Roberts, G.N. and Taylor, I.N. (2006), Weed management practices in glyphosate-tolerant and conventional cotton fields in Australia. *Aust J Exp Agric* 46, 1177-1183.

Whitburn, G. and Downes, S. (2009). Surviving *Helicoverpa* larvae in Bollgard II® :Survey results. *The Australian Cottongrower Magazine* 30, 12-16.

Whitehouse, M.E.A. (2011). IPM of mirids in Australian cotton: Why and when pest managers spray for mirids. *Agricultural Systems* 104, 30–41.

Whitehouse, M., Wilson, L. and Fitt, G. (2005). A comparison of arthropod communities in transgenic Bt and conventional cotton in Australia. *Environmental Entomology* 34, 1224-1241.

Wilson, L.J., L.R. Bauer, and G.H. Walter. (1996). 'Phytophagous' thrips are facultative predators of two-spotted spider mites (Acari: Tetranychidae) on cotton in *Australian Bulletin of Entomological Research* 86, 297–300.

Wonkeun, Park, Brian E. Scheffler, Philip J. Bauer and B. Todd Campbell. (2012). Genome-wide identification of differentially expressed genes under water deficit stress in upland cotton (*Gossypium hirsutum* L.) *BMC Plant Biology*, 12; 90.

Wu K.M., Lu, Y.H., Feng, H.Q., Jiang, Y.Y. and Zhao, J.Z. (2008). Suppression of cotton bollworm in multiple crops in China in areas with Bt toxin-containing cotton. *Science* 321: 1676–1678.

Xiao, J., K. Wu, David D. Fang, David M. Stelly, John Yu and Roy.G. Cantrell (2009). New SSR Markers for Use in cotton (*Gossypium* spp.) improvement. *The Journal of Cotton Science*, 13; 75–157.

Xiao, Y.H., Li, D.M., Yin, M.H., Li, X.B., Zhang, M., Wang, Y.J., Dong, J., Zhao, J., Luo, M., Luo, X.Y., Hou, L., Hu, L. and Pei, Y. (2010). Gibberellin 20-oxidase promotes initiation and elongation of cotton fibers by regulating gibberellin synthesis. *Journal of Plant Physiology*, 167; 829-837.

Xie, F., Sun, G., Stiller J.W. and Zhang, B. (2011). Genome-wide functional analysis of the cotton transcriptome by creating an integrated EST database. *PLoS ONE*, 6: e26980

Yeates, S., Roberts, J. and Richards, D. (2010). High insect protection BIOTECH Bt cotton changes crop morphology and response to water compared to non Bt cotton. *In* Food Security from Sustainable Agriculture. Edited by H. Dove *Proceedings of 15th Agronomy Conference 2010*, 15-18 November 2010, Lincoln, New Zealand. http://www.regional.org.au/au/asa/2010.

Yu, J. Z., Russell J. Kohel, David D. Fang, Jaemin Cho, Allen Van Deynze, Mauricio Ulloa, Steven M. Hoffman, Alan E. Pepper, David M. Stelly, Johnie N. Jenkins, Sukumar Saha, Siva P. Kumpatla, Manali R. Shah, William V. Hugie, and Richard G. Percy. (2012). A High-Density Simple Sequence Repeat and Single Nucleotide Polymorphism Genetic Map of the Tetraploid Cotton Genome. G3. The Genetics Society of America, 2; 143-58.

Zhang, L., Fu-Guang Li, Chuan-Liang Liu, Chao-Jun Zhang and Xue-Yan Zhang. (2009). Construction and analysis of cotton (*Gossypium* *arboreum* L.) drought-related cDNA library. *BMC Res Notes*, 2:120.

Zhang Mi., Xuelian Zheng, Shuiqing Song, Qiwei Zeng, Lei Hou, Demou Li, Juan Zhao, Yuan Wei, Xianbi Li, Ming Luo, Yuehua Xiao, Xiaoying Luo, Jinfa Zhang, Chengbin Xiang and Yan Pei. (2011). Spatiotemporal manipulation of auxin biosynthesis in cotton ovule epidermal cells enhances fiber yield and quality. *Nature Biotechnology*, 29; 453–458.

Zhao, C.X., Guo, L.Y., Jaleel, C.A., Shao, H.B. and Yang, H.B. (2008). Prospects for dissecting plant-adaptive molecular mechanisms to improve wheat cultivars in drought environments. *Compt Rend Biol J* 331: 579- 586.

Annex I

Highlights of Presentations and Feedback from Members for the Meeting held on September 4, 2011

Australia is strictly employing refuge crop requirement to avoid the development of resistance to endotoxins as well as herbicide tolerance. Resistance is continuously monitored and additional options like heavy tillage are also employed to delay development of resistance. Of course, there is a cost involved in the implementation of resistance management strategies, but it is worth making these investments. The reduced use of insecticides in Australia in clear in the form of a continuous decline in endosulfan contents in river water. Australia is already working on the Resistance Management Plan for Bollgard III technology before it is approved for commercial use. (Adam Kay, Australia)

India has greatly benefitted from insect resistant biotech cotton in terms of higher yields. India is at the final stages of testing Roundup Ready cotton. India has experienced the following issues as a consequence of adopting biotech cotton.

1. With the introduction of biotech cotton in India, the focus on hybrids having biotech genes has increased significantly. Consequently, a smaller number of hybrids dominate the planting seed market. The area under traditional diploids species and extra fine cotton has been squeezed to a minimum, threatening the production of short staple cotton.
2. India was proud to have a large and experienced team of cotton breeders. The adoption of biotech cotton has affected the tradition of having a competent and strong team of conventional breeders.
3. The reduced use of insecticides has resulted in an increase in secondary pests like mealybug.
4. The high price of biotechnology is of concern to Indian growers. The Government of India had to intervene to regulate the technology fee, and farmers are now charged a technology fee fixed by the Government.

The first two events of biotech cotton have been used extensively, and it is time to think beyond insect resistance and herbicide tolerance on issues like marker-assisted selection. (C. D. Mayee representing Keshav Kranthi, India)

Dr. Keshav Kranthi further emphasized this issue via email following the meeting:

‘Though the benefits of biotech have been commendable, the next generation future plans appear to be undefined. Since almost all the biotech technologies were driven from the private multinational companies, the future plans may have been shrouded in secrecy. It is time that proper investment is made to strengthen public sector efforts in biotech cotton with solid collaborative technical plans between interested cotton growing countries for common good, which will then create possibilities for low cost products and long term sustainability.’

In Colombia, biotech cotton is more popular among large growers compared to small growers.

The high cost of the technology is of concern to Colombian growers. The cost of seed increased by 23% in one year in 2010/11. (Mr. Eduardo Roman representing Mr. Jairo Palma, Colombia)

In Argentina, biotech cotton arrived on the market in 1998 with Bollgard in a foreign variety. Adoption improved when the Round up Ready trait was incorporated in a local variety from INTA in 2001. Adoption reached around 90% at present. Most cotton farmers cultivate small areas. The high cost of biotech cotton may explain the extended use by small farmers of seed from informal markets that prevent them from taking full advantage of biotechnology. To cope with the problem of the informal market, government, seed companies, local multipliers and the cotton industry have recently reached an agreement to facilitate the access of small farmers to certified biotech seeds at lower prices. However, biotechnology in the cotton seed market is ineffective against boll weevil, which is the main production constrain for small farmers. (Fernando Ardila, Argentina)

Monsanto always analyzes the conditions suitable for adoption of biotech cotton very carefully. Monsanto makes sure that a country must have cultivation practices suited to growing biotech cotton, must have biosafety regulations in place, must be affected by target insects to be controlled and the country must allow import of biotech products as food and feed before offering commercial adoption of a biotech event. The candidate country must abide by patent laws and respect intellectual property rights and other intellectual frameworks. (Miguel Alvarez Arancedo, Monsanto, Argentina)

Dr. Bill Norman, USA talked about trade issues that restrict transportation of commercial goods and technologies across borders. In particular he brought up the following issues for consideration by the Round Table.

1. Asynchronous international approval processes – In some cases certain products are approved in one country while others have to wait several years. Dr. Norman suggested parallel path for approval of new products.
2. Adventitious presence issues – Some countries restrict importation of products with zero tolerance for biotech products. In case of violations, penalties are severe under local laws.
3. Coexistence with organic and other production systems – Some specialty cottons prohibit the use of biotech cotton.

Biosafety laws and regulations used as trade barriers – Biosafety regulations in some countries have specific barriers and ambiguities that are detrimental to international trade. (Bill Norman representing Keith Menchey, USA)

Brazil took time to commercialize biotech cotton because of the regulation problems. The area that is suitable for planting of biotech cotton without risk to wild species of cotton has been mapped. Embrapa based this map on three years of research. Now, all biotech events approved in the world are approved in Brazil (Bollgard, Bollgard II, Wide Strike, Roundup Ready, Liberty Link, Gly Tol, Bollgard + Roundup Ready, Twin Link). Biotech cotton was planted on about 260,000 ha, and the perspective for 2012 is about 600,000 ha of biotech cotton. Embrapa is introducing the genes Roundup Ready Flex and Bollgard II in local varieties. According to researchers and producers, the main benefits of biotech cotton are fewer sprays (reductions of at least two sprays per season) and reduced complexity of cultural practices. There is a perception of fewer sprays with the new biotech events that were recently approved. The use of biotech in cotton in Brazil in the next few years will be a marketing issue rather than a regulation problem. (Alderi Emidio de Araujo representing Paulo Augusto Vianna Barroso, Brazil)

Over 50 people from different countries attended the open meeting of the Round Table. Questions and comments from the floor are summarized below:

- Why has Australia not commercialized biotech canola?
- Is the emergence of secondary pests as major pests an epistatic effect of the Bt gene inserted in varieties?
- The need for coordination rises with the level of technology adopted.
- Biotech cotton should be grown as a part of a production system.
- Intercropping with crops susceptible to glysophate is not feasible with Roundup Resistant cotton.

Future Plans

A closed meeting of the Round Table members decided the following plan for implementation.

1. The ICAC Secretariat will prepare a report on the meeting, in collaboration with the Chair of the Meeting Dr. Fernando Ardila, and send it to all members.
2. Dr. Keith Menchey, Chair of the Round Table will contact all members and ask them to submit a 'summary issue' in the form of a 3-5 pages report.
3. Dr. Menchey in collaboration with the Secretariat will consolidate 'summary issues' in the form of a report based on consolidation of ideas and setting priorities.
4. The report will be distributed to all members, and if need be the ICAC Secretariat will organize a conference call. Email communications will continue in any case.
5. The consolidated report, if found appropriate, will be finalized as a report of the Round Table. If there is a need for more discussions/communications, the report will be discussed by the Round Table at the 71st Plenary Meeting in Switzerland in October 2012.

Topics allocated on November 17, 2011

Adam Kay	- Limitations and prospects of sharing biotech products
Eduardo Roman/Jairo Palma	- Implications of non-target pests in biotech cotton
Osama Momtaz	- Biosafety regulations and public education
Hans Willemse	- Technology fee
Abdel Bagi	- Technology expectations and prospects
Keith Menchey/Bill Norman	- Trade implications and other issues of concern
Keshav Kranthi	- Upstream technologies
Tassawar Hussain Malik	- Concerns from growers
Paulo Barroso	- Lessons learnt in the last 15 years: Merits and challenges
Fernando Ardila	- Labeling and technical aspects with potential impact on the international trade

Annex II

Aid Memoire
Round Table for Biotechnology in Cotton

14:30 hr. Sunday, October 7, 2012
Chair by: Dr. Keith Menchey, Chairman of the Round Table for Biotechnology in Cotton, USA

Dr. Keith Menchey of the National Cotton Council of America chaired the meeting. Members/representatives from Argentina, Colombia, Pakistan, South Africa and ICAC provided summaries of their reports. The meeting was open to the public and about 100 people from various countries attended and participated in the discussion. The major highlights of the meeting included the following:

1. Biotech cotton has benefited growers across countries but the benefits have not been uniform. Colombia and South Africa reported that some regions have availed higher benefits compared to others. Dryland cotton has not realized the same benefits as irrigated particularly under South African cotton growing conditions.
2. Secondary pests that were of less economic importance in the past have become an issue in the absence of insecticide spraying against Lepidoptera species.
3. Biotech cotton should be introduced through local varieties. Imported biotech varieties not adapted to local conditions have shown detrimental characteristics such as poor germination and lower yields.
4. While ICAC does not have access to the agreements signed by individual governments and technology providers, ICAC will provide information on recent changes in technology fees and publicly available information on specific revisions to the required conditions to commercially grow biotech cotton.
5. Most countries expressed concern that, even though the benefits of the technology have declined over the years, technology fees remain the same or have even increased in some cases.
6. There are high expectations for new traits to be approved in cotton with reference to the drought tolerant corn that has been deregulated in the USA from 2012, hope to have drought tolerant cotton in the next few years seems to be genuine.
7. Regulatory processes are hindering the adoption of biotech cotton into more countries, particularly the developing countries.
8. There is a need for the public sector to give higher emphasis to research in the field of biotechnology. Governments must invest in biotechnology to lower the cost of the technology and to ensure food security.
9. Burkina Faso reported that it has benefited from biotech cotton in many ways. There was a high level of interest in the success story of Burkina Faso. ICAC will arrange an English translation of the Burkina Faso country statement to the 71st Plenary Meeting of the ICAC and make it available on the web.
10. In the USA, growers provide feedback to the technology providers through Grower Advisory Committees which meet several times per year. Such direct interaction with the technology providers is lacking in many countries.

Following the general meeting a closed meeting of the Round Table members was held. The following decisions were made in this meeting.

1. There are some duplications in the reports/contributions from various members. Duplication will be identified and combined.
2. Information from the country report of Burkina Faso to the 71st Plenary Meeting of the ICAC will be utilized in the report. Similarly, information from countries that are not represented on the Round Table will be solicited for inclusion in the report.
3. There are a number of issues for which countries have reached common conclusions. Such conclusions and issues will be summarized in a separate section.
4. Members realized that the first draft of the report is still deficient/weak in certain areas. It was decided that such areas will be identified and additional information will be included in the report.
5. The Round Table also decided to maintain the format in such a way that it will capture the impact and experiences of various countries while providing a congruent document.
6. The Round Table members also decided that the report would be a continuation of the work of the previous ICAC Expert Panels on biotechnology in cotton.