An Analysis of the Development and Regulation of Agricultural Biotechnology in Pakistan

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Andrew Roberts[Δ]*, Hina Nazli[Ω], Michael Wach[Δ], Yusuf Zafar[†].

[Δ] A. Roberts and M. Wach, Agriculture & Food Systems Institute, Center for Environmental Risk Assessment
[Ω] H. Nazli, Research Fellow, Pakistan Strategy Support Program, IFPRI
[†] Y. Zafar, Director General, Agriculture and Biotechnology Division, Pakistan Atomic Energy Commission

*To whom correspondence should be addressed. Email: aroberts@foodsystems.org.

INTRODUCTION

Since the first commercial production of genetically engineered (GE) plants in the mid-1990s, the use of these plants in agriculture has expanded to include millions of acres in both developed and developing countries. Along with the potential for benefit from the adoption of improved GE varieties, most countries consider the potential for risks to the environment that may be posed and regulate their introduction. Although the term is imprecise, environmental regulation for the safe development and commercial application of GE plants has come to be referred to as 'biosafety' regulation. This is distinct from considerations of food safety which may be associated with the products of GE plants, although it does incorporate some consideration of human health associated with environmental exposures.

In Pakistan, a significant investment has been made in technologies and research to support the development of indigenous GE plants. In addition, Pakistan is a Party to the Cartagena Protocol on Biosafety which requires, among other things, that decisions related to the movements of LMOs across borders (*i.e.*, transboundary movement) be informed by a risk assessment. In response to this, and other domestic and international obligations, the Government of Pakistan (GoP) has promulgated a biosafety regulatory system. This system has been in operation since 2005 and has achieved some success in regulating the introduction of GE plants in Pakistan, particularly in allowing field trials under confined conditions.

The purpose of this analysis is to present the context for biosafety regulation in Pakistan, including the investment and infrastructure currently dedicated to advanced agricultural technologies, and to review the legal and regulatory framework present in the country. It presents the historical context for the introduction and regulation of Bt cotton, the only GE plant to receive commercial regulatory approval in Pakistan, as well as reviewing some of the challenges facing the biosafety system. Finally, it looks at opportunities for advancing the biosafety regulatory system in order to improve the ability of the government and people of Pakistan to adopt technologies that will bring benefit to Pakistani agriculture while ensuring an adequate level of protection for the environment.

REVIEW OF THE BIOTECHNOLOGY RESEARCH SECTOR IN PAKISTAN

The development of GE plants is one activity in a continuum of research and development that can be collectively considered 'agricultural biotechnology.' As such, neither the research and development nor the regulation of these plants should be considered in isolation. Efforts in Pakistan for agricultural improvement through the use of advanced technologies have been supported with both domestic and international assistance and this section reviews both historic and ongoing efforts at agricultural technology development in order to provide context for the regulation of GE plants in Pakistan.

HISTORY OF AGRICULTURAL BIOTECHNOLOGY IN PAKISTAN

The advent of traditional biotechnology in Pakistan was initiated in the Botany Department of Peshawar University in the 1970s. Professor Dr. Ihsan Ilahi established a plant tissue culture facility for the medicinal plants *Rauwolfia serpentine,*[1] Papaver,[2] and many more. Later the areas of bio-fertilizer (Biological nitrogen fixation – BNF and mycorhizza, etc.) and bio-pesticides (neem extracts and bio-control methods) along with tissue culture of vegetatively grown crops (banana, date palm, potato, sugarcane and many other horticultural plants) were initiated in various university departments and research organizations in the public sector. These activities have continued for decades in those centers and a few products derived from this work, like virus free potato seeds, multiplication of healthy banana, sug-

1 Akram and Ilahi *et al.* 1986.

2 Ilahi and Ghauri 1994.

arcane and date palm plants have been commercialized.[3] Similarly many production units of bio-fertilizers in both the public and private sectors are operating in the country.[4] Likewise bio-control activities for insects in sugarcane fields in Sindh are expanding, with the help of the sugar industry, and represent a globally recognized success story. Most of the departments are still pursuing research and development in the above stated sectors. These endeavors, though extremely useful, have not been able to attract private sector investment. Recently the USAID-sponsored Agribusiness Support fund (www.agribusiness.org.pk) resulted in the establishment of a banana tissue culture facility at Nizamani farms in Sindh. Similarly, the public-private sector partnership of NIA, Tandojam and sugar industry in Sind resulted in the establishment of ten production sites for rearing biological control organisms for use by sugarcane growers. The real success story is in bio-fertilizer production units which have been developed at a huge investment. This sector is flourishing due to the higher cost of synthetic fertilizers and a ban on the movement of nitrogenous fertilizer in the restive tribal areas.

The role of biotechnology as an engine of growth and socio-economic development in Pakistan has been recognized in all key policy documents of the GoP (www.pc.gov.pk). Despite low investment in research and development[5] for the national agriculture sector, research and development for agricultural biotechnology received a fairly good share of this meager resource. However the funding in the public sector was not sustainable.

The challenges of food security in Pakistan are enormous due to rapid increase in population, declining share of fresh water and arable land and ever-rising input costs of agro-chemicals and energy. All these challenges are expected to become more daunting in the wake of climate change.[6]

The first National Science and Technology (S&T) policy of Pakistan was formulated in 1984. The subjects of Molecular Biology, and Genetic Engineering were placed in priority research areas.[7] Later, in 1997, some modification was made and the National Technology Policy was launched maintaining an emphasis on biotechnology as one of the priority areas (Zafar 1997, Zafar 2002). Keeping in view the rapid pace of advancements in S&T taking place around the world, the GoP initiated the process of formulating its new S&T policy in 2009 later named 'National Science, Technology & Innovation Policy (ST&I - 2011) of Pakistan'.[8] This policy also placed biotechnology and genetic engineering among the priority areas. This policy has been vetted by the Law and Justice Ministry and was officially launched in November, 2012. It is pertinent to note that the recent devolution process did not affect the Ministry of Science and Technology (MoST) as science and technology was designated a federal subject.

Other related polices include cotton vision 2010, cotton vision 2015 and now the new cotton policy 2030, the latter of which is under active formulation by the Ministry of Textile and clearly mentions biotechnology as an important tool for enhanced and sustainable productivity of the cotton crop (http://www.textile.gov.pk/). Similarly the Agriculture Policy of GoP also recognized the importance and application of biotechnology in improving this sector. However, it is clear from these policy documents that there is no single ministry or focal point in the government (unlike, for example, the Department of Biotechnology of India). Various ministries (Agriculture, Education, Environment, Health, Textile and Science and Technology) and research organizations, (PAEC, PARC, HEC, NIH, PMRC, etc.) launched biotech programmes with little or no co-ordination. This resulted in the dilution of otherwise meager resources and duplication of research activities. This in turn reduced the ability of research activities to have visible and significant socio-economic impact resulting from biotechnology except in a few selected areas like molecular diagnostics and genetically modified (GM) cotton release in the country. Some policy interventions have recently been made to translate laboratory work into commercial enterprise. HEC recently asked all public sector universities to have an Office of Research, Innovation and Commercialization (ORIC) on campus to provide a one window operation for entrepreneurs. Three universities (HEJ/Karachi University, NUST - Islamabad and UVAS-Lahore) are in the process of developing industrial or biotech parks to launch high value, small volume industrial units by utilizing the research and development resources of the university.

BIOTECHNOLOGY CENTERS IN PAKISTAN

The importance of the vast potential of agricultural biotechnology was formally recognized in 1981 when the first training course on recombinant DNA technology was organized at the Nuclear Institute for Agriculture and Biology (NIAB), Faisalabad, Pakistan, one of the three agricultural centers of the Pakistan Atomic Energy Commission (PAEC). This The U.S. National Science Foundation (USNSF) sponsored workshop recommended the establishment of an exclusive National Center of Biotechnology and Genetic Engineering. Meanwhile, the United National Industrial Development Organization (UNIDO) initiated efforts to establish an International Centre for Genetic Engineering and Biotechnology (ICGEB), and Pakistan applied for locating such a center in the country. Two review missions visited Pakistan for evaluation, and Pakistan was short listed.

3 Zafar 1997.

4 Hafeez 2009, Hafeez and Hassan 2012.

5 The GoP invested 0.29% of Agricultural GDP back into agricultural research in 2003 (the latest year for which statistics are available). Compare this to India and Bangladesh, which invested 0.36% of Agricultural GDP (2003 and 2002 respectively), China which invested 0.49% (2007) or Brazil which invested 1.66% (2006). Figures taken from http://www.asti.cgiar.org/.

6 http://www.pc.gov.pk/vision2030/approach%20paper/t5/theme%205-M%20E%20Tasneem-1.pdf

7 Khan 1997.

8 http://www.pcst.org.pk/docs/National%20Science,%20Technology%20and%20Innovation%20Policy%202012.pdf

Unfortunately ICGEB was not built in Pakistan,[9] and instead was divided into two parts, located in New Delhi, India, and Trieste, Italy. Biotechnology research has been carried out at many of the research centers in Pakistan. Although these centers have some of the scientific capabilities needed to use biotechnological tools, the research efforts are comparatively small.[10] Most of the centers still lack a sufficient number of trained researchers and adequate financial resources to mount large scale research programs.[11] Presently, there are 34 government institutes and universities working broadly in agricultural biotechnology (Table 1), however modern biotechnology research (including the development of genetically engineered plants) is restricted to only a few of the major centers, like National Institute for Biotechnology and Genetic Engineering (NIBGE), Center of Excellence of Molecular Biology (CEMB), National Agriculture Research Center (NARC) and Forman Christian College University (Table 2). It is pertinent to note that all research and development activities in agricultural biotechnology in Pakistan are being carried out in the public sector only and genetic engineering is now an integral part of the agriculture sector in Pakistan.[12]

COMMODITY/CROPS

It is interesting to note that a GM crop development program was initiated in chickpea and rice at CEMB, Lahore during 1984-94. GM rice (Bt) was finally developed in mid 1990s and even evaluated in field for biosafety purpose.[13] Many attempts to generate Bt-chickpea were made[14] however; no field testing was ever conducted. Like chickpea, ambitious programmes on mango and citrus were shelved due to serious problem encountered in tissue culture of these fruit trees. CEMB however continued to consolidate pioneering work on indigenous gene development. At present the center is one of the leading plant biotechnology groups in the country. GM cotton developed by CEMB has already been through the field testing and approval stage. Similarly GM potato, tomato and rice are also at advanced phases of development.

During the same time (1984-94), the plant tissue culture sector of NARC launched a development programme for GM potato, rice, tomato and sugarcane for various traits[15] however; none of the material was ever tested in the field. Various administrative changes badly affected the activities of biotech groups of NARC. It was once the largest research group in NARC with 17 researchers having foreign Ph.D. degrees and training in plant biotechnology. A recent initiative to create the National Institute for Genomics & Advanced Biotechnology (NIGAB) has allowed the reconstitution of the groups and development of GM wheat, chickpea and groundnut is in process.[16]

The epidemic of cotton leaf curl virus in 1992-3 attracted major funding to the plant biotechnology sector. NIBGE, Faisalabad launched a programme on GM virus resistant cotton which was later expanded to various other traits. For a long time, 1994-2004, NIBGE, Faisalabad remained focused on GM cotton and developed excellent expertise in transformation of Coker 312 (model cotton crop). However, it is interesting that the first GM crop development project (1992-96) at NIBGE was GM rice with the Xa21 gene acquired from the International Rice Research Institute (IRRI) through a material transfer agreement (MTA). The GM basmati rice was developed[17] but shelved due to possible trade ban of GM rice for export to EU countries. NIBGE is presently working on development of GM cotton, wheat, potato and sugarcane. All these materials in the greenhouse and/or field testing phase.

KIBGE in Karachi also launched a GM brassica and wheat development programme which is at green-house stage. Similarly Forman Christian College University (FCCU, Lahore) also launched GM wheat for quality traits. The putative GM wheat plants are in green house.

TRAITS EMPLOYED FOR GM CROPS

Indigenous cloning of insect resistant novel genes from bacteria was the first project taken up by CEMB, Lahore (1984-94). The group surveyed various areas of Pakistan (from Karachi to Gilgit) and collected >600 isolates of *Bacillus* species, performed molecular characterization and identified various useful genes for plant genetic engineering. This capability of isolating genes and constructing indigenous vectors for plant genetic engineering is a hallmark of the centre.[18] CEMB, Lahore is employing locally produced Cry1Ac, Cry2Ac for insect resistance, EPSPS for herbicide tolerance, waxy genes for drought tolerance and many other genes for abiotic stress tolerance (www.cemb.edu.pk).

NIBGE, Faisalabad also developed the capability to produce their own gene constructs. For virus resistant projects, NIBGE followed the route of 'pathogen derived resistance' and thus isolated and cloned 3-5 genes of cotton leaf curl virus (CLCuV) in various combinations and transformed them into cotton.[19] The first batch of GM virus resistant cotton plants were field tested but failed as a new virus mutant (CLCuV- Burewala) emerged in the field. RNAi technology was also acquired in collaboration with Sainsbury Labs, UK (Prof. David Baulcomb) and various constructs were developed for virus re-

9 Zafar 1997.

10 Atanassov *et al*. 2004, Broerse 1990, De Silva 1997.

11 Khan and Afzal 1997, Masood 1995, Zafar 2002.

12 Zafar 2007.

13 Bashir *et al*. 2004.

14 Husnain *et al*. 1997.

15 Rashid *et al*. 1996, Khan *et al*. 2003, Nyla *et al*. 2009.

16 Iqbal *et al*. 2011.

17 http://www.nibge.org

18 Mahmood-ur-Rahman *et al*. 2007.

19 Asad *et al*. 2003.

Table 1. Departments/Institutes of Biotechnology in Pakistan.

Sr. No.	Centre	Website	Year	Academic/ Res.	GM Crop Program
1	Institute of Biotechnology and Genetic Engineering (IBGE), Agricultural University Peshawar	http://aup.edu.pk/	2000	Yes/Yes	Yes
2	Centre for Animal Biotechnology, Veterinary Research Institute, Pakhtunkhwa/North-West Frontier Province (NWFP), Peshawar		1996	No/Yes	animal vaccine/ diagnostic
3	Centre of Biotechnology, University of Peshawar, Peshawar	www.uop.edu.pk	2000	Yes/Yes	No
4	National Institute for Genomics and Advanced Biotechnology (NIGAB), National Agricultural Research Centre (NARC), Islamabad	www.parc.gov.pk	2007/1986	Yes/Yes	Yes
5	Institute of Biomedical and Genetic Engineering, KRL General Hospital, Islamabad	www.uok.edu.pk	1994		No
6	Department of Biosciences, Comsats Institute of Information Technology (CIIT), Islamabad Campus, Islamabad	www.comsats.edu.pk	2000	Yes/Yes	Yes (recently)
7	Department of Environmental Sciences, International Islamic University, Islamabad	www.iiu.edu.pk	2007	Yes/Yes BS/MS Biotechnology	No
8	Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad	www.qau.edu.pk	2006	Yes/Yes	Yes
9	Institute of Biochemistry and Biotechnology, University of Arid Agriculture, Rawalpindi	http://www.uaar.edu.pk	1998/2011	Yes/Yes	No
10	School of Biological Sciences (SBS), University of the Punjab(PU), Lahore	www.pu.edu.pk	2004	Yes/Yes	Yes
11	Department of Microbiology and Molecular Genetics, PU, Lahore	www.pu.edu.pk	2002	Yes/Yes	No
12	Institute of Industrial Biotechnology, Government College University, Lahore	www.gcu.edu.pk/bio_tech.html	2005	Yes/Yes	No
13	Biotechnology and Food Research Centre, Pakistan Council for Scientific and Industrial Research (PCSIR) Laboratories, Lahore	www.pcsir.gov.pk	1977	No/Yes	No
14	Centre of Excellence in Molecular Biology (CEMB), PU, Lahore	www.cemb.edu.pk	1985	Yes/Yes	Yes
15	Institute of Agriculture Sciences (IAGS), PU, Lahore	www.pu.edu.pk/iags	2002	Yes/Yes	No
16	Institute of Biochemistry and Biotechnology, University of Veterinary and Animal Sciences, Lahore	www.uvas.edu.pk/institutes/ibbt/	2006/ 2009 (merger of two departments)	Yes/ Yes	animal genomics/ diagnostic
17	Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore	www.uol.edu.pk/faculty/imbb/index.html	2004	Yes/Yes	No
18	Department of Biotechnology, Lahore College for Women University, Lahore	www.lcw.edu.pk	2010	Yes/Yes	No
19	Department of Biotechnology, Kinnard College for Women University, Lahore	www.kinnaird.edu.pk	2010	Yes/Yes	No
20	Department of Biotechnology, Foremen Christian College, Lahore	www.fccollege.edu.pk	2009	Yes/Yes	Yes
21	Institute of Biochemistry and Biotechnology (IBB), PU, Lahore	www.pu.edu.pk	1997	Yes/Yes	
22	Agriculture Biotechnology Research Institute (ABRI), Faisalabad	www.agripunjab.gov.pk	1987	No/Yes	Yes
23	Centre for Agriculture Biochemistry and Biotechnology (CABB), University of Agriculture, Faisalabad	www.uaf.edu.pk	1996	Yes/Yes	No
24	Institute of Biotechnology, Bahauddin Zakaria University, Multan	http://www.bzu.edu.pk/index.php?id=25	2006	Yes/Yes	In collaboration with CEMB
25	Biochemistry and Biotechnology Department, Islamic University, Bahawalpur	www.iub.edu.pk	2009	Yes/Yes	No
26	Biotechnology Department, Agriculture University, Tando Jam Sindh	www.sau.edu.pk	2006	Yes/Yes	No
27	Institute of Biotechnology and Genetic Engineering (IBGE) Sindh University, Jamshoro, Sindh	www.usindh.edu.pk	2002	Yes/Yes	No
28	Institute of Biochemistry, University of Balochistan, Quetta	www.uob.edu.pk	1986	Yes/Yes	No
29	Biotechnology Division, International Center for Chemical and Biological Sciences (ICCBS), HEJ Research Institute, University of Karachi (KU), Karachi	www.iccs.edu	1998	Yes/Yes	Yes
30	Dr. A.Q. Khan Institute of Biotechnology and Genetic Engineering (KIBGE,) KU, Karachi	www.uok.edu.pk www.kibge.edu.pk	2006	Yes/Yes	Yes
31	National Centre for Proteomics, KU, Karachi	www.incp.uok.edu.pk	2008	Yes/Yes	No
32	Dr. Punjwani Centre for Molecular Medicine and Drug Research, KU, Karachi	www.uok.edu.pk	2008	Yes/Yes	No
33	Department of Biotechnology, KU, Karachi	www.uok.edu.pk	1996	Yes/Yes	No
34	Department of Enviornmental Sciences, CIIT, Abbotabad, KPK	www.comsats.edu.pk	2011	Yes/Yes	No

Table 2. Major institutes engaged in developing GM crops in Pakistan.

No.	Institute	Containment Facility
1	National Institute for Biotechnology and Genetic Engineering (NIBGE)	Yes
2	Centre of Excellence on Molecular Biology (CEMB)	Yes
3	Plant Biotechnology, ICCBS/HEJ, Karachi University, Karachi	Under construction
4	National Institute for Genomics and Advanced Biotechnology(NIGAB), NARC, Islamabad	Yes
5	School of Biotechnology(SBS), University of the Punjab, Lahore	No
6	Institue of Biotechnology and Genetic Engineering (IBGE), Agriculture University, Peshawar	No
7	Agriculture Biotechnology Research Institute(ABRI), AARI, Faisalabad	Yes (small)
8	Quaid-i-Azam University, Islamabad	No
9	Foremen Christian College, Lahore	Yes (small)

Table 3. Crops undergoing transformation in Pakistan.

Crop	Institute
Cotton	CEMB, Lahore; NIBGE, Faisalabad; IAGS, Lahore; NARC, Islamabad
Brassica	IBGE ,Peshawar; KIBGE, Karachi; ABRI/AARI, Faisalabad
Rice	CEMB, Lahore; NIBGE, Faisalabad; NARC, Islamabad; SBS PU, Lahore
Wheat	NIBGE, Faisalabad; F.C. College, Lahore; CABB/UAF, KIBGE, Karachi; NARC, Islamabad
Potato	NIBGE, Faisalabad; QAU, Islamabad
Ground Nut	NARC, Islamabad; University of Arid Agriculture, Rawalpindi
Chickpea	CEMB, Lahore (abandoned); NARC, Islamabad; CIIT, Islamabad (Pea)
Sugarcane	NIBGE, Faisalabad; SBS PU, Lahore
Tomato	NIBGE, Faisalabad; NARC, Islamabad; QAU, Islamabad
Chili	NIBGE, Faisalaba; Quaid-i-Azam University, Islamabad
Soya bean	Quaid-i-Azam University, Islamabad

sistance in chili,[20] cotton[21] and for male sterility in tomato for hybrid seed production.[22] NIBGE received recognition for isolating a novel insect resistance gene from Australian Web spider (HvT) which was small in size (4 kD) as compared to Cry1Ac (68 kD) and also has a different target site (calcium channel of nervous system). This was employed to develop insect resistant tobacco (a model plant).[23] HvT was patented in Pakistan in 2008. However, the generation of extensive biosafety data for this novel gene hindered the field testing. NIBGE recently identified a strong group of genes utilizing bio-informatics tools to mine databases that are in the public domain with a view to local construction of indigenous gene cassettes. Thus, gene constructs of salt/ drought tolerance (AVPI, AtNHXI, LfNHX1); herbicide tolerance (EPSPS); and insect resistance (Cry1Ac, Cry2Ab, ViP, Hvt) have been developed and placed in model plants (tobacco) and crops of interest.[24]

A strong group in NIBGE is also developing cDNA libraries of cotton as well as of *Calotrpis procera* which has long fiber on its seed.[25] This research is endeavoring to provide a wealth of new genes AND some specific promoters for genetic engineering. This should provide a strong foundation for obtaining genes of desired traits indigenously.

In addition to the two major groups in the country, CEMB and NIBGE, some other groups are emerging. The Institute of Biochemistry and Biotechnology of University of Arid Agriculture, Rawalpindi is involved in the isolation of genes through modern biotechnology tools. The group first isolated various genes of banana bunchy top virus (BBTV) for developing pathogen derived resistance in banana for Sindh region (Hyder *et al.* 2007) and then germin like protein for biotic/abiotic stress tolerance.[26] The group also patented selected genes with the patent office in Pakistan.[27] Another recent addition is the Institute of Agricultural Sciences (IAS) at

20 Shafiq *et al*. 2010.

21 Hashmi *et al*. 2011.

22 Nawaz-ul-Rehman *et al.* 2007.

23 Khan *et al*. 2006.

24 Asad *et al*. 2008, Ibrahim *et al*. 2009, Mubin *et al*. 2007, Saeed *et al*. 1997, Sohail *et al*. 2012.

25 Indrais *et al*. 2011.

26 Dunwell *et al.* 2008, Mahmood *et al.* 2007.

27 http://www.ipo.gov.pk

Punjab University.[28] The researchers at IAS, in collaboration with the University of Toronto in Canada, developed some novel gene constructs for developing virus resistant cotton.

Very recently a new group emerged in Foremen Christian College University (FCCU) in Lahore.[29] This group is working on improvement of wheat for uptake and availability of iron. They targeted phytic acid (binding compound of iron) through phytase. The gene cassette was developed at NIBGE and placed in wheat. These two research projects have been liberally funded by Punjab Agriculture Research Board, Lahore.[30]

Most of the above groups are also employing several other genes, like DREB series, AVPI, AtNHX1, Cry1Ac, Cry2Ab, ViP, Chitinase and many others which were either acquired through MTAs from various universities in the USA, Japan and Germany or collected from the labs where researchers obtained their Ph.D.s or spent time as post docs. It is pertinent to note that the first release of Bt cotton in the country harboured MON531 event for Cry1Ac of Monsanto. It was extensively exploited as the gene (Cry1Ac) and/or event (MON531) had not been patented in Pakistan.

ROLE OF PRIVATE SECTOR

In Pakistan, the fertilizer and agro-chemical sectors have been separated from government control and are instead run by the private sector through national and multi-national companies (MNC). Major MNCs like Monsanto, Bayer Crops Sciences, Dupont-Pioneer, Syngenta, FMC, ICI-Astra Zeneca, Nichimen (now Arysta Life Science) and several Chinese companies have a prominent presence both in the agro-chemical and seed sectors. There are more than 600 national seed companies also operating in the country. Most of them are just distributors while very few (4-6) have some reasonable research and development capacity. MNCs also import advanced lines and multiply/evaluate them in the country. Out of 155 cases submitted to NBC, four cases by Monsanto on GM cotton and GM corn, two cases by Bayer Crops Sciences on GM cotton, two cases by Dupont Pioneer for GM corn and two cases by Syngenta also for GM corn are being field tested to fulfill all the criteria of biosafety and contained field testing.

Among national seed companies, Ali Akbar Company, Lahore in collaboration with CEMB, Lahore submitted cases of GM cotton with 2-3 genes of insect resistance and herbicide tolerance (Cry1Ac, Cry2Aa and EPSPS). Another national seed company, Guard Seed Company, made collaboration with an Indian seed company (Nath Seeds) and got approval of hybrid Bt cotton (Cry1Ac + Cowpea trypsin, inhibitor-CPTI), which was originally developed by Bio-century of China. A public sector seed company, Punjab Seed Corporation (PSC, Lahore), signed an MoU with Silver Land Company of China to develop GM cotton especially insect resistant cotton. Several national seed companies are launching projects under public-private partnerships which include Allahdin Group of Companies, Multan with PARC, 4B Group of companies with CEMB, Lahore and Jhallander seed company, Rahimyar Khan with NIAB, Faisalabad to acquire research based advanced materials for evaluation, selection and commercialization. Another company, Augira Chemical Company, developed collaboration with Hubei Seed Company, China to bring hybrid rice and GM cotton into the country.

In the present scenario, seed dealers in Pakistan as well as an informal sector of seed developers, so called 'progressive farmers', are making substantial profits with little or no investment in research and development.[31] The weak Seed Act, 1976, poor implementation of patent rules and absence of plant varietal protection regulations are major hurdles in the development of a viable and responsive private seed sector in the country. Though financial risks are high, some MNCs and a few major national seed companies are proceeding with research and development because the Pakistan seed sector is large and offers huge potential for business. Proposed amendments to the Seed Act, 1976 and promulgation of the Plant Breeder Rights Act are intended to strengthen the private seed sector and attract foreign direct investment for the benefit of the farmers. At present, the private seed sector is flourishing exclusively in the hybrid seed sector (sunflowers, canola, corn and fodders). This is happening despite all the weakness in the system as 'technology barriers' provide enough of a safeguard for the investment. For example, MNCs use GM traits in hybrid corn to avoid the risk of illegal multiplication and piracy. Pakistan is a founding member of WTO and thereof of TRIPS[32] agreement. The patent rules were modified to encompass microbes, genes, vectors, etc., by intellectual property organization of Pakistan[33] and first promulgated in 2000-2002.

MNCs have re-acquired patents for these genes in Pakistan to avoid piracy and infringement. However, the weak capacity of IPO-Pak is another reason for ineffective implementation; although due administrative and legislative rules and regulations have been incorporated in the IPR ordinance. So far private seed companies have obtained licenses from Chinese companies (Bio-century, Hubei Seed Company, Silver Land and Xin Xiang Seed Company) and only one with Indian seed compound (Nath Seed) for utilization of insect resistant genes for cotton. No agreement yet had been made by any MNCs (Monsanto, Bayer Crop Sciences, Syngenta and Dupont-Pioneer) with any public or private organization in Pakistan.

INTERNATIONAL COLLABORATIONS

Pakistan is a founding member of International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy. The

28 http://pu.edu.pk/home/department/53

29 www.fccollege.edu.pk

30 http://parb.punjab.gov.pk/

31 Abdullah 2010, Rana 2010.

32 See subsequent discussion of the TRIPS agreement under WTO Obligations.

33 www.ipo.gov.pk

Table 4. Development/deployment of GM crops in Pakistan by the private sector (foreign)

COTTON

Company	Trait	Event	Partner	Year of Start	Stages	Current Status
Monsanto	Insect + herbicide (stacked)	MON531 + MON1598 and MON1445	Nil Imported hybrid from Mahyco Monsanto India	2008	3 confirmed field trials completed. Hybrid cotton imported from India every year	Waiting for NBC approval for deregulation/ commercialization
Bayer Crop Science, Germany	Insect + herbicide (stacked)	Monsanto events + resistance Glufosinate (bar) gene	Nil Imported from Bayer Crop Science, India	2010	2 confirmed field trials at designated location Hybrid cotton imported from India every year	One year field trial left for deregulation evaluation/approval
Nath Seed Corporation, India	Insect resistance	Cry 1Ac + CpTl (Chinese origin Bio-Century)	Private sector Guard Seed Corporation, Lahore	2007	Many confined field trials Hybrid cotton imported from India every year	Approval for commercialization in May 2010
Silver Land, China	Insect resistance	Cry 1Ac + CpTl (Chinese origin)	Public Punjab Seed Corporation, Lahore	2009	Back Cross Breeding OPV/confined field trials	Not submitted to NBC for commercialization
Heibei Seed Company, China	Insect resistance	Cry 1Ac + CpTl (Chinese origin)	Private Auriga Seed Company, Lahore	2009	Back Cross Breeding OPV/confined field trials	Submitted the case for approval to NBC. Decision pending

CORN

Company	Trait	Event	Partner	Year of Start	Stages	Current Status
Monsanto, USA	Herbicide + insect	MON event	Nil Hybrid imported from USA	2010	Confined field trial	Approval (deregulation) case pending with NBC/EPA. More data demanded
Syngenta, Switzerland	Herbicide + insect resistance	Nil Hybrid imported from Purte Rico	Nil Hybrid imported from Puerto Rico	2011	Confined field trial	One year. More field trials are required
Dupont-Pioneer Hi-bred USA	Herbicide + Insect resistance	MON events + Dupont events	Nil Hybrid imported from USA	2010	Confined field trial	One year. More field trials are required

Source: NBC/EPA, Ministry of Climate Change, Government of Pakistan

National Institute for Genetic Engineering and Biotechnology (NIBGE, Faisalabad) is the focal point of this multi-lateral, international organization. ICGEB is sponsoring research projects, training, workshops and even transfer of genes through MTA (Cry1Ac, Cry2Ab and Vip) to some research organizations in Pakistan. The Rockefeller Foundation also sponsored two biotech rice projects at NIBGE, Faisalabad and CEMB, Lahore (1986-95). At the same time, the US National Academy of Sciences (USNAS) also sponsored BOSTD – PARC linkage programmes and awarded several projects on plant biotechnology to many national research and development organizations. The major contributions in human resources development were made in 1986-96 era when USAID under MART project provided M.Sc./Ph.D. and long term training in the agricultural sector. NIBGE, Faisalabad received 15 exclusive scholarships for Ph.D.s/long term training from USAID – MART in the area of biotechnology. This was further strengthened by Asian Development Bank and International Cotton Advisory Committee (ICAC) and Common Funds for Commodity (CFC) funded projects on 'Management of Cotton Leaf Curl Virus' in which major groups in the USA (University of Arizona; Donald Danforth Plant Science Center, St. Louis; Texas A&M University) and John Innes Centre, UK exchanged expertise and material in national cotton biotechnology program. In fact, this laid a very strong foundation for plant biotechnology (genomics, molecular diagnostic and genetic engineering) in the country. The bilateral projects under Pak-Australia (ACIAR), Pak-China and PAK-USA (USNAS-HEC/MoST & PSSP for cotton, wheat and foot and mouth disease (FMD) in livestock all have a fair share of plant biotechnology projects. Other donor agencies (FAO, Fulbright Foundation, IAEA, World Bank, ABD, IFS, COMSTECH, OIC, IDB-Jeddah) also contributed in developing human resources, infrastructure and research projects in the field of agricultural biotechnology. Recently NIBGE provided a vector for developing virus resistant chickpea to ICARDA, a vector for virus resistant tomato to the University of Arizona and one for developing

virus resistant banana to INIBAP, France under MTA. These initiatives have recently been taken and indicate the potential for biotechnology programs in Pakistan.

EXPERIENCE WITH THE REGULATION OF AGRICULTURAL BIOTECHNOLOGY IN PAKISTAN: A LOOK AT BT COTTON

PRODUCTION OF COTTON IN PAKISTAN

Cotton production is important to Pakistan's agriculture and the overall economy. Nearly 26 percent of all farmers grow cotton, and over 15 percent of Pakistan's total cultivated area is devoted to this crop, with production primarily in two provinces: About 79 percent of total cotton production takes place in Punjab, 20 percent in Sindh and the remaining 1 percent in the other two provinces.[34] Cotton and its products (yarn, textiles and apparel) contribute significantly to the gross domestic product (8%), total employment (17%), and, particularly, foreign exchange earnings (54%) of the country.[35] In addition, the cotton seed is used in edible oil and livestock feed. Cotton picking, mostly done by females, provides supplementary income to rural farm and non-farm households. A large proportion of the employed population is engaged in the textile manufacturing sector. Because of their extensive forward and backward linkages, the cotton-textile sectors have important implications for national economic performance and poverty reduction.[36]

Cotton production is a high risk activity. From sowing to harvest, various pests attack the roots, leaves, stems and fruit of the cotton. Pest infestation is the major cause of yield losses in the cotton crop. These pests can be divided into two categories: 'sucking pests' (e.g., aphids, jassids, thrips, mites, white fly, and mealy bug), and 'chewing pests' (e.g., cotton bollworms, spotted bollworms, pink bollworms, etc.). In Pakistan both types of pests are common. Since the early 1990s, cotton production in Pakistan has been facing the challenge of large-scale pest infestation that has been contributing to unexpected fluctuations in cotton yield and significant economic losses. A wide range of pesticides has been introduced to control various cotton pests during the last 15 years, which has increased yields but also notably increased the cost of cotton production. Moreover, as the pests have developed resistance to these chemicals, their effectiveness has declined over time. Given the economic importance of this crop, cotton research has always received a high priority in Pakistan. The primary objective of cotton research has been to develop new cotton varieties that are resistant to pests, heat and drought, and have high yield potentials with desirable fiber characteristics. Because of huge crop losses, despite achieving varietal improvement, Pakistan still has not been able to achieve its full potential for cotton production. The data on cotton and textile indicates that the textile sector expanded at a higher rate than the cotton sector. As a result Pakistan spends nearly US$ 0.5 billion per year on the imports of cotton lint. The current yield of seed-cotton produces 11.6 million cotton bales of 170 kg. The domestic consumption by the textile sector is 15.5 million bales. Therefore, to meet the current domestic demand, there is a need to increase the production of cotton lint at least by 3.9 million bales (i.e., an increase of 34%). Pakistan can become an exportable country again if yield increases by 40 percent. Currently, seed-cotton yield in Pakistan is around 2000 kg per hectare. Among the top five cotton producing countries this yield is much lower than that in China, Brazil or USA and only exceeds the yield in India. High pest infestation and cotton diseases are the main causes. Estimated losses vary from 10-15 percent in a typical year to 30-40 percent in a bad crop year.[37] The vulnerable farm households can be pushed into poverty in a bad crop year by high crop losses.[38] By controlling the crop losses, Pakistan can increase the yield per hectare.

GM COTTON IN PAKISTAN

Genetically modified (GM) varieties of cotton provide a potentially significant means for addressing the issue of crop loss by controlling certain pest infestations. Currently available GM cotton varieties incorporate one or more genes from a naturally occurring, soil-borne bacterium called *Bacillus thuringiensis* (Bt) into the tissue of a cotton variety. These are sometimes referred to collectively as 'Bt cotton'.

THE ROLE OF MULTINATIONALS

Monsanto has played a central role in the introduction of genetically modified cotton worldwide, starting in the US in 1996. The commercial production of GM varieties is conditional on a fee paid to the owners of the gene. This 'technology fee' is charged at a specified rate per hectare. Countries can obtain GM technology either by developing a system to transform genotypes, or by purchasing the technology through partnership with public or private with companies that own the genes. Most of the developing countries do not have the resources to develop a research system for isolating their own genes, so they purchase the technology from the gene owner.

To promote collaborative research in advanced transgenic technology, the Government of Pakistan (GoP) signed a letter of intent (LOI) with Monsanto on May 13, 2008. To allow the commercial production and distribution of the latest Bt cotton seed in a regulated market, the GoP then started negotiations with Monsanto. After several meetings and negotiations, the GoP signed an agreement with Monsanto in March 2009 to import hybrid seed from India and in April 2010 signed a memorandum of understanding with Monsanto

34 Government of Pakistan 2003.

35 Government of Pakistan 2009, 2011.

36 Cororaton and Orden 2008.

37 Salam 2008.

38 The operated land of most of the farmers is less than five hectares. They have limited access to information, technology, and credit. There exists a wide difference in the yield obtained on medium/large versus small farms. For example, the average yield per hectare of seed-cotton on small farms is 1,700 kg, whereas medium/large farms on average can produce 3,500 kg per hectare (Arshad 2009).

for introducing Bollgard-II technology. However, due to a disagreement over the high technology fee, the contract regarding the preparation and distribution of the latest GM seed using the germplasm of Pakistan's cotton varieties could not be approved.[39]

LEGALIZED RELEASE OF GM COTTON: REGULATORY CONSTRAINTS IN PAKISTAN

Among the four largest cotton producing countries, Pakistan has been slowest to approve the commercialization of GM cotton. USA has been growing GM cotton since 1996, China since 1997, and India commercialized this crop in 2002. Despite having in place administrative procedures required for the approval of a GM crop,[40] Pakistan legalized commerce in its first GM crop (cotton) in 2010.

Pakistan initiated work on GM cotton in 1995. However, the process of drafting the biotechnology legislation has remained extremely slow. For example, the draft of the Pakistan Biosafety Guidelines was submitted to the Ministry of Environment in January 2000. However, enactment of these guidelines only came into force after the approval of the Pakistan Biosafety Rules in 2005.[41] The Plant Breeders' Rights Bill, 2008 and the Seed (Amendment) Bill, 2008 have yet to be approved by the parliament. The delay in the regulatory process in Pakistan resulted in the cultivation of unapproved and unregulated varieties of Bt cotton, developed locally using Monsanto's transformation event MON531.[42] Because of the fear of a lawsuit and trade sanctions if patent infringement is established none of the varieties was submitted to the National Biosafety Committee (NBC) for approval until 2007.[43] In addition, National Institute of Biotechnology and Genetic Engineering (NIBGE), the leading institute in biotechnology research in Pakistan, developed a Bt variety in 2004 using the event MON531. The variety was submitted to the NBC for approval. However, considering the issue of infringement of Monsanto's patent, the NIBGE withdrew its case from the NBC. Until 2008, the plant breeders and molecular biologists did not know that Monsanto did not have patent protection on MON531 in Pakistan and they could use this transformation event. Because of the lack of awareness of these facts, they were reluctant to formally approach the regulatory authorities for biosafety assessment. In 2008, after the establishment of the fact that Monsanto did not have a patent on MON531, local public and private breeders submitted their cases to the NBC. The lack of awareness about biotechnology laws is another important reason for the delay in adoption of biotech crops. In sum, slow legislative process; cumbersome procedures for the development, approval, testing and commercialization of biotech products; lack of skilled human resources; and weak research infrastructure are the major factors hindering the approval of Bt cotton.[44]

STATUS OF BT COTTON IN PAKISTAN (AS OF MARCH 2012)

The National Biosafety Committee (NBC) approved eight domestically developed Bt varieties for field testing in March 2009. Among these varieties, two varieties used the gene isolated by the local scientists indigenously.[45] All other varieties used the transformation event MON531. In 2010, Pakistan formally approved ten cotton varieties and one cotton hybrid and the first commercial Bt crop was cultivated in 2010-11. In addition, Chinese seed/biotech companies made contract agreements with private companies as well as with public sector institutes for the importation of GM seeds. However, despite the legalized release of GM crop, the implementation of the Plant Breeder's Rights Act and amendments to the Seed Act are still pending in the parliament.

Most recently, in January 2012, the Government of Punjab dropped the idea of introducing Bt cotton seed in collaboration with Monsanto. The Government of Punjab argues that the primary threats facing the cotton crop in Punjab are sucking pests such as white fly, mealy bug, and jassids. Bt cotton does not provide protection from these pests. Therefore, it is anticipated that signing a contract with Monsanto by paying a technology fee may not bring benefits.[46] A recent analysis indicates that obtaining Bt technology by paying technology fee may not be a wise decision if the effectiveness of this technology in the form of decline in pesticide expenditure is less than 10 percent and increase in yield is not more than 20 percent. However, if Bt cotton can control pests effectively and is able to increase yield, the latest Bt technology, even at high technology fee, will be beneficial for Pakistan.[47]

In February 2012, the Punjab Seed Council approved four new Bt cotton varieties for cultivation in Punjab, and four Bt varieties were approved for one year for field performance/monitoring of the varieties. In addition, three varieties were commercialized after the completion of one year successful field trials. Eight varieties were deferred by the Punjab Seed Council.[48]

39 Monsanto agreed to grant the license to the government of Pakistan for the use of technology in Pakistani varieties; the government would then sub-license it to the public and private seed companies if the agreement materialized. The two parties did not reach an agreement.

40 Administrative and research efforts include biosafety rules and biosafety guidelines, intellectual property rights (IPRs) systems, and field trials.

41 Zafar 2007.

42 According to an estimate, Bt varieties account for almost 100 percent cotton area cultivated (USDA 2010).

43 Government of Punjab 2008.

44 Nazli 2010.

45 The variety CEMB-1 contains a single gene and CEMB-2 contains double genes. Both genes were developed indigenously at the Centre of Excellence in Molecular Biology (CEMB).

46 News item published in the daily 'The News', January 3, 2012.

47 Nazli 2010.

48 News item published in the daily 'The News', February 18, 2012.

CONCLUSION

Despite considerable progress in preparing the regulatory framework for agricultural biotechnology, the capacity of the regulatory bodies has remained weak. As a result, first GM crop (cotton) approval was issued in 2010. However, the commercialized varieties are using the Monsanto's transforming event of the first generation of GM crops and are lacking the latest traits. Due to the high and increasing pressure of sucking pest on the cotton in the largest growing province, Punjab, the Government of Punjab dropped the idea of acquiring latest Bt cotton seed in collaboration with Monsanto by paying a technology fee. In addition, the Plant Breeders' Rights Bill and the Seed Amendment Bill are still awaiting approval from the parliament.

LEGISLATIVE CONTEXT

As in other countries, the development of agricultural biotechnology in Pakistan occurs in the context of a legal framework consisting of laws, regulations and guidelines that interact with science, technology and the environment in different ways. The following section looks at two relevant Acts that have implications for the development and regulation of agricultural biotechnology. The analysis here is of the Acts as they are written and does not attempt to address their implementation in Pakistan.

PAKISTAN ENVIRONMENTAL PROTECTION ACT OF 1997

The Pakistan Environmental Protection Act of 1997 (the Act) was enacted to provide for the 'protection, conservation, rehabilitation and improvement of the environment', 'prevention and control of pollution', and the 'promotion of sustainable development'. The Act incorporates an all-encompassing definition of the *environment*,[49] so that few aspects of the outside world are exempt from the Act's authority. However, in spite of its potential breadth, the Act's apparent focus is on the protection of the environment from harms caused by hazardous substances.[50]

The Act establishes a multi-tiered hierarchy of administrative bodies, beginning with the Pakistan Environmental Protection Council, which is responsible for setting and implementing national environmental policy. The Council is also empowered to direct any government agency to take action that will further the goals of the Act. Enforcement of the Act is the responsibility of the Pakistan Environmental Protection Agency (EPA). The EPA is granted numerous enforcement powers, including investigatory and subpoena powers; the power to issue search warrants and environmental protection orders; and the authority to take environmental samples and confiscate property—activities appropriate for the management of emergency situations where a hazardous substance is leaking into the environment and must be stopped as quickly as possible. In addition, each provincial government is directed to establish a provincial environmental protection agency, and the coordination of the provincial agencies is also the responsibility of the EPA, managed through the National Environmental Co-ordination Committee.

Each province is directed to create a provincial sustainable development fund, using monies from federal grants and loans, as well as provincial funds. The funds may be used to provide financial assistance for projects designed to further the underlying goals of the Act: improvement and protection of the environment, sustainable resource development, and environmental research. The funds are managed by Provincial Sustainable Development Fund Boards.

In practice, the Act is concerned with the identification of adverse environmental effects that may result from proposed projects and the prevention or mitigation of such effects. The *proponent* of a project may be anyone, a natural person or a legal entity, such as a corporation or governmental body, and the *project* is 'any activity, plan, scheme, proposal or undertaking involving any change in the environment'.[51] A central principle underlying the Act is that projects must not be allowed to go forward unless the proponent of the project has either determined that the project is unlikely to result in adverse environmental effects, after preparing an *initial environmental examination* (IEE), or the proponent has evaluated the effects likely to occur by preparing an *environmental impact assessment* (EIA).[52]

The preparer of an IEE must review the reasonably foreseeable impacts of the project and determine whether these impacts will result in adverse environmental effects.[53] If no adverse effects are found, the analysis is complete. If adverse effects are deemed likely, the project proponent must prepare an EIA. The preparation of an EIA is a much more complicated process involving the collection of relevant data, the comparison of project alternatives, the formulation of a comprehensive environmental management plan for the project, and submission of recommendations. Little guidance is provided as to the preparation of these documents, except that the Act requires

49 Environment is defined as the aggregation of 'air, water and land'; 'all layers of the atmosphere'; 'all organic and inorganic matter and living organisms'; 'the ecosystem and ecological relationships'; 'buildings, structures, roads, facilities and works'; 'all social and economic conditions affecting community life'; and 'the inter-relationships between any of the factors' above.

50 Pesticides are specifically excluded from the definition of hazardous substance.

51 However, the examples of projects provided in the Environmental Protection Act are all related to construction, except for one, 'any change of land use or water use'.

52 "No proponent of a project shall commence construction or operation unless he has filed with the Government Agency designated by Federal Environmental Protection Agency or Provincial Environmental Protection Agencies, as the case may be, or, where the project is likely to cause an adverse environmental effects an environmental impact assessment, and has obtained from the Government Agency approval in respect thereof." Section 12(1)

53 An "'initial environmental examination' means a preliminary environmental review of the reasonably foreseeable qualitative and quantitative impacts on the environment of a proposed project to determine whether it is likely to cause an adverse environmental effect for requiring preparation of an environmental impact statement." Section 2(xxiv)

public participation in the preparation of EIAs, and the Act requires government review of EIAs and as well as decision to approve or reject them within four months of submittal. Any 'aggrieved person' may make a written complaint to an Environmental Tribunal in the event a project proponent is required to prepare an EIA but fails to do so.

Currently, the Act lists three specific adverse effects, namely impairment of or damage to 'human health and safety', 'biodiversity', and 'property', but the Act does not refer to agriculture or agricultural biotechnology. However, all three of these resources are routinely examined in the context of the potential effects of agricultural biotechnology, and of course, the development and commercial release of the products of agricultural biotechnology involve a 'change of land use or water use', one of the types of projects specifically mentioned by the Act. So, while the Act appears to focus on traditional concepts of environmental pollution, it does provide a framework on which to base the regulation of agricultural biotechnology and its products.

THE SEED ACT, 1976

The goals of the Seed Act are to promote the development of, and protect the integrity of, the seed production industry, through the regulation of crop varieties and the certification of seed. Although the Seed Act creates a comprehensive system to achieve these goals, the scope of the Seed Act is limited to organizations established by the Provincial governments to produce seed: private companies are not mentioned by the Act.

Like the Environmental Protection Act, the Seed Act establishes a multi-tiered hierarchy of governing bodies, with different functions and varying levels of authority. At the top is the National Seed Council, which sets policy for the seed industry, approves seed quality standards, assists the development of new seed production farms, and regulates inter-provincial seed movement. The Federal Seed Certification Agency registers seed growers and controls overall seed quality. In addition, the Agency appoints seed inspectors, who audit seed production facilities and collect samples for analysis. Finally, the National Registration Agency determines the suitability of new varieties for registration, registers new seed varieties, and publishes a list of official varietal descriptions.

Each provincial government must, under the terms of the Seed Act, establish a Provincial Seed Council. Each Council determines which registered varieties are of agricultural value to growers in the province. Such varieties are called 'released' varieties.' Provincial Councils also recommend local growers for registration as seed producers by the Federal Seed Certification Agency.

These bodies work together to enable the production and sale of 'notified' seed varieties. The notification, which is published in the official Gazette, describes the variety; lists the province(s) where it may be produced; specifies the minimum germination rate and purity of the seed; and determines the labeling which must be affixed to the seed container. Once this occurs, no one may represent a container of seed to be of a notified variety unless all the above requirements are met. A network of government-appointed seed inspectors, seed certification officers, and seed analysts then work to ensure Seed Act compliance.

Seed inspectors and certification officers[54] have considerable authority and can enter and search seed production facilities, examine records, take samples for analysis, and take custody of seed lots not meeting the standards set down for that variety. In addition to the loss of the seed, violators of the Seed Act face monetary fines and even imprisonment for repeat offenses.

As mentioned above, the Seed Act does not address commercial plant breeding and seed production by private companies, nor does it discuss the types of breeding methods to be used. The Seed Act precedes the advent of plant biotechnology, but not of mutagenesis, both of which are now commonly used in the development of new crop plant varieties. Proposed amendments to the Seed Act have been under consideration by the legislature for several years, and it is likely that an amendment to address modern biotechnology is under consideration.

INTERNATIONAL OBLIGATIONS FOR AGRICULTURAL BIOTECHNOLOGY

The movement of agricultural products across international boundaries represents a substantial value for Pakistan and the rest of the world. This movement of produce and commodities, including those incorporating agricultural biotechnology, is addressed by international agreements and Pakistan is both a member of the World Trade Organization (WTO) and a party to the Cartagena Protocol on Biosafety to the Convention on Biological Diversity. The next section considers the obligations imparted by these two agreements and their ramifications for consideration of biosafety in Pakistan.

WTO OBLIGATIONS RELATED TO AGRICULTURAL BIOTECHNOLOGY

The World Trade Organization (WTO) was established in 1995 as a result of the Uruguay Round of trade negotiations (1986-1994), and earlier negotiations under the General Agreement on Tariffs and Trade (GATT). The WTO serves as a forum to negotiate trade agreements and to settle disputes related to trade, including trade in agriculture and thus agricultural biotechnology. Like the GATT before it, the WTO enshrines among its members an obligation to pursue policies that allow for open trade between nations, and that are not unduly restrictive. 155 member countries are part of the organization (as of March 2012) and Pakistan was a founding member, joining the WTO on January 1, 1995. Obligations related to agricultural biotechnology stemming from the WTO are derived primarily from

54 Seed certification officers differ from seed inspectors only in that inspectors are supervised by certification officers.

the Agreement on the Application of Sanitary and Phytosanitary measures (the SPS agreement) and may also be impacted by the Agreement on Technical Barriers to Trade (TBT agreement). The Agreement on Trade Related Aspects of Intellectual Property Rights, or 'TRIPS' agreement is not related to biosafety or risk assessment. However, it is worth mentioning because it does apply to intellectual property aspects related to agricultural biotechnology.

The SPS Agreement

The SPS agreement addresses measures to protect human and animal health, and phytosanitary issues (plant health). This includes restrictions on the importation of plants and animals or their products for the purpose of the prevention of the introduction of plant an animal pests. Although the agreement does not specifically mention agricultural biotechnology, it applies widely to any measures intended to protect human, animal, or plant health including the movement of agricultural products.

Several principles of the WTO are confirmed in the SPS agreement. Article 2 paragraph 1 confirms the right of countries to develop and apply national rules that protect human, animal and plant health,[55] while paragraph 2 of the same article confirms an obligation to take the least trade restrictive measures available to achieve that protection as well as an obligation to base measures on scientific principles and evidence.[56] Paragraph 3 confirms members' obligation to apply measure without discrimination. Any measures taken to restrict trade must be applied equally and fairly to all other countries, and must be applied equally within the states and territories of each country as well.[57]

Risk assessment is required to support SPS measures, and the provisions governing those assessments are set out in Article 5. These require that risk assessments be based on available scientific evidence and be conducted in accordance with any appropriate international guidance (paragraph 1). Paragraph 5 requires that measures must be consistently applied with respect to levels of protection,[58] while paragraph 7 allows for the adoption of restrictive measures in the face of uncertainty, provided those measures are provisional and the necessary scientific evidence is collected within a reasonable amount of time.[59]

The TBT Agreement

The TBT agreement deals with 'technical regulation', which is defined as any 'document which lays down product characteristics or their related processes and production methods, including the applicable administrative provisions, with which compliance is mandatory. It may also include or deal exclusively with terminology, symbols, packaging, marking or labelling requirements as they apply to a product, process or production method'. This intersects more narrowly with biosafety considerations for agricultural biotechnology than the SPS agreement, and is generally considered relevant only for production method conformity and for labeling requirements. These latter are not biosafety concerns, although they may be addressed in national policy for agricultural biotechnology.

Experience with Agricultural Biotechnology under the WTO

The application of WTO provisions to the regulation of agricultural biotechnology has been tested by a dispute between the United States and the European Union. Although the details of the case are complex, the results of the dispute panel confirmed that the general provisions of the WTO and specifically the requirements under the SPS agreement for risk assessment and scientific justification for protective measures apply in the case of agricultural biotechnology.[60]

THE CARTAGENA PROTOCOL ON BIOSAFETY

The Cartagena Protocol on Biosafety (the Protocol) is an agreement under the Convention on Biological Diversity that specifically addresses the safety of 'Living Modified Organisms' or LMOs in the environment in relation to international trade. LMO is defined as 'any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology'. Drafted in 1999-2000, the Protocol entered into force in 2003 and currently (as of March 2012) has 163 parties. Pakistan signed the Protocol in 2001, but did not deposit the instruments of ratification until March, 2009. The objective of the Protocol is to ensure the safe transfer,

55 "Members have the right to take sanitary and phytosanitary measures necessary for the protection of human, animal or plant life or health, provided that such measures are not inconsistent with the provisions of this Agreement."

56 "Members shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence, except as provided for in paragraph 7 of Article 5."

57 "Members shall ensure that their sanitary and phytosanitary measures do not arbitrarily or unjustifiably discriminate between Members where identical or similar conditions prevail, including between their own territory and that of other Members. Sanitary and phytosanitary measures shall not be applied in a manner which would constitute a disguised restriction on international trade."

58 "With the objective of achieving consistency in the application of the concept of appropriate level of sanitary or phytosanitary protection against risks to human life or health, or to animal and plant life or health, each Member shall avoid arbitrary or unjustifiable distinctions in the levels it considers to be appropriate in different situations, if such distinctions result in discrimination or a disguised restriction on international trade. Members shall cooperate in the Committee, in accordance with paragraphs 1, 2 and 3 of Article 12, to develop guidelines to further the practical implementation of this provision. In developing the guidelines, the Committee shall take into account all relevant factors, including the exceptional character of human health risks to which people voluntarily expose themselves."

59 "In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organizations as well as from sanitary or phytosanitary measures applied by other Members. In such circumstances, Members shall seek to obtain the additional information necessary for a more objective assessment of risk and review the sanitary or phytosanitary measure accordingly within a reasonable period of time."

60 For details and current status on Dispute 291 see http://www.wto.org/english/tratop_e/dispu_e/cases_e/ds291_e.htm

handling and use of LMOs that may have an adverse impact on the conservation and sustainable use of biological diversity in the context of transboundary movements (i.e., movement between countries or jurisdictions).[61] The Protocol has 39 articles and three annexes, but for the purposes of discussion these confer a relatively simple set of obligations on Parties.

Advance Informed Agreement

Articles 7, 8, 10, and 12 confer an obligation on Parties to follow an Advance Informed Agreement (AIA) procedure for the first transboundary movement of any LMO intended for environmental release in the Party of import. Taken together, these articles require the Party of export to notify (or require the exporter to notify) the competent national authority in the Party of import, who may then make a decision on whether or not to allow the import, in accordance with a risk assessment undertaken pursuant to Article 15 and Annex III. The Protocol only requires the AIA procedure to be followed for the first transboundary movement of a particular LMO to the Party of import, but Article 10 reserves the right of the Party of import to determine whether the procedure will apply to subsequent transboundary movements. LMOs that are imported for direct use as food, feed or for processing (FFP) are not considered to be intended for introduction into the environment, and are specifically exempted from the requirement of AIA and therefore decisions related to the import of LMO FFPs do not require a risk assessment pursuant to the Protocol.

Risk Assessment under the Protocol

The Protocol directly addresses risk assessment for LMOs in Article 15 and in Annex III. Article 15 states that risk assessments must be carried out in a scientifically sound manner and in accordance with Annex III. Annex III states that the objective of risk assessment is to identify and evaluate the potential adverse effects of LMOs on the conservation and sustainable use of biological diversity in the likely receiving environment, and lays out a set of general principles for conducting risk assessment. These include that risk assessments should be scientifically sound and conducted in a transparent manner, that risks associated with LMOs should be considered in the context of risks posed by their non-modified counterparts and that risk assessments should be conducted on a case-by-cases basis taking into account the specific characteristics of an LMO and its intended use. Annex III also proscribes basic methodology to follow in conducting the risk assessment and lays out some 'points to consider' which may apply to a risk assessment depending on the specific case. The full text of Annex III is provided in the box on page 14.

61 The full text of Article 1: Objective : "In accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements."

Additional Obligations under the Protocol

A number of other obligations are enshrined in the Protocol, most having to do with administrative responsibilities for notifying decisions, reporting to the Conference of the Parties and monitoring implementation of the Protocol. Article 2, paragraph 1 requires that 'Each Party shall take necessary and appropriate legal, administrative and other measures to implement its obligations under this Protocol.' At the first Conference of the Parties serving as the Meeting to the Parties, associated with Decision BS-I/5 on Capacity Building, an Action Plan was drafted which included a list of priorities for capacity building. One of these was providing assistance for the development of national biosafety frameworks. Over time and with the prevalence of capacity building under the UNEP Global Environment Facility (GEF) in this regard, it has become widely believed that a National Biosafety Framework is required as an obligation under the Protocol. This is not the case, as the Protocol simply requires that Parties have appropriate capacity to implement the obligations under the Protocol, whatever form that capacity may take.

PERCEIVED CONFLICT BETWEEN THE WTO AND THE PROTOCOL

There is a widely held perception that the agreements of the WTO and the provisions of the Protocol are in conflict with respect to their treatment of agricultural biotechnology. This may be due to the fact that the primary purpose of the WTO is to facilitate trade while the Protocol aims to protect the conservation and sustainable use of biodiversity. The perception is likely exacerbated by the fact that many large agricultural producers that make use of agricultural biotechnology (Argentina, Australia, the United States, and Canada) are not Parties to the Protocol. However, the WTO agreements explicitly acknowledge the right of members to adopt protective measures to prevent damage to the environment and the preamble to the Protocol recognizes that environmental and trade agreements should be mutually supportive. An examination of the text of relevant articles and paragraphs between the two instruments reveals many similarities among them, especially the requirement for sound, science-based risk assessment in support of decision making.

Some of the perceived conflict is related to differing interpretations of the precautionary approach as laid out in Principle 15 of the Rio Declaration on Environment and Development. The Protocol affirms the precautionary approach in both the preamble and Article 1 and the full text is provided below.

The Precautionary Approach (Principle 15, Rio Declaration on Environment and Development, full text)

In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.

FULL TEXT OF ANNEX III OF THE CARTAGENA PROTOCOL ON BIOSAFETY

Objective

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

Use of risk assessment

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

b) General principles

3. Risk assessment should be carried out in a scientifically sound and transparent manner, and can take into account expert advice of, and guidelines developed by, relevant international organizations.

4. Lack of scientific knowledge or scientific consensus should not necessarily be interpreted as indicating a particular level of risk, an absence of risk, or an acceptable risk.

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

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

Methodology

7. The process of risk assessment may on the one hand give rise to a need for further information about specific subjects, which may be identified and requested during the assessment process, while on the other hand information on other subjects may not be relevant in some instances.

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

a) An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health;

b) An evaluation of the likelihood of these adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism;

c) An evaluation of the consequences should these adverse effects be realized;

d) An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized;

e) A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks; and

f) Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment.

Points to consider

9. Depending on the case, risk assessment takes into account the relevant technical and scientific details regarding the characteristics of the following subjects:

10. a) **Recipient organism or parental organisms.** The biological characteristics of the recipient organism or parental organisms, including information on taxonomic status, common name, origin, centres of origin and centres of genetic diversity, if known, and a description of the habitat where the organisms may persist or proliferate;

b) **Donor organism or organisms.** Taxonomic status and common name, source, and the relevant biological characteristics of the donor organisms;

c) **Vector**. Characteristics of the vector, including its identity, if any, and its source or origin, and its host range;

d) **Insert or inserts and/or characteristics of modification.** Genetic characteristics of the inserted nucleic acid and the function it specifies, and/or characteristics of the modification introduced;

e) **Living modified organism.** Identity of the living modified organism, and the differences between the biological characteristics of the living modified organism and those of the recipient organism or parental organisms;

f) **Detection and identification of the living modified organism.** Suggested detection and identification methods and their specificity, sensitivity and reliability;

g) **Information relating to the intended use.** Information relating to the intended use of the living modified organism, including new or changed use compared to the recipient organism or parental organisms; and

h) **Receiving environment.** Information on the location, geographical, climatic and ecological characteristics, including relevant information on biological diversity and centres of origin of the likely potential receiving environment.

The text indicates that protective measures can be adopted to prevent serious or irreversible damage and that lack of full scientific certainty is not required before cost-effective measures may be taken. Predictably, interpretations vary wildly on what damage to the environment is 'serious or irreversible', what level of scientific certainty may or may not be required to justify protective measures and what a 'cost-effective measure' may be with respect to the environment. Some countries and stakeholders favor an interpretation of the precautionary approach whereby no action should be taken with respect to the environment without full scientific certainty that no damage would occur. In addition to being logically problematic, this interpretation is clearly in conflict with the SPS agreement of the WTO's requirement for scientific justification of trade disrupting measures.[62] It is important to note, however, that such an extreme interpretation of the precautionary approach is not required by either the Rio Declaration or the Protocol, and that there is no inherent conflict between the treaties. The SPS agreement explicitly acknowledges the rights of members to adopt interim protective measures while collecting scientific information to better understand the potential for damage provided these measures are not put in place solely to disrupt trade.

THE PAKISTAN BIOSAFETY SYSTEM (PRIOR TO JUNE, 2011)

Prior to the devolution of Federal Ministries in 2010 and 2011, the Pakistan Biosafety system was defined by two instruments: The Pakistan Biosafety Rules and the Biosafety Guidelines. These were implemented, at least in part, in response to the signing by Pakistan of the Cartagena Protocol on Biosafety. The following section reviews the text of these instruments. Implementation is discussed earlier, in the review of experience with Bt cotton and later in the discussion of the challenges currently facing the biosafety system.

PAKISTAN BIOSAFETY RULES, 2005

The Pakistan Biosafety Rules (the Rules) were notified in 2005, citing section 31 of the Pakistan Environmental Protection Act as the authorizing law. As discussed above, the Environmental Protection Act does not explicitly mention biotechnology, but because section 31 of the Act empowers the Federal Government to make rules to carry out the purposes of the Act, the Rules acknowledge the authority of the Government over biotechnology.

The Rules are applicable to three broad, frequently overlapping categories of organisms and activities:[63]

a) Manufacture, import and storage of micro-organism and gene technological products for research whether conducted in laboratories of teaching and research, research and development institutes or private companies involved in the uses and applications of genetically modified organisms and products thereof;

b) All work involved in the field trial of genetically manipulated plants, animals (including poultry and marine life), micro-organisms and cells; and

c) Import, export, sale and purchase of living modified organism, substances or cells and products thereof for commercial purposes.

Although the Rules incorporate the definition of *modern biotechnology* used in the Cartagena Protocol on Biosafety, many of the terms used in the above categories are not defined in the Rule, and thus the scope of the Rule may be open to interpretation. For example, it is unclear as to whether paragraph (a) means that the Rules apply to all microorganisms or only genetically modified ones; and no examples are provided to indicate the types of activities covered by the term *work*, mentioned in (b). However, the Pakistan Environmental Protection Agency has subsequently provided guidance on the scope of the Rule, interpreting the three paragraphs, taken together, to mean that the Rules are applicable to laboratory research, field trials, and commercial release of genetically modified (GM) plants, GM animals, and GM microorganisms, as well as any commercial transactions involving these organisms.[64]

The Rules establish a three-tiered hierarchy of governing bodies designated to administer the Biosafety Rules. The National Biosafety Committee (NBC) and the Technical Advisory Committee (TAC) are Federal-level committees, and the third tier comprises all the Institutional Biosafety Committees (IBCs) that have been created within the various institutions that are engaged in regulated biotechnology activities.

There is considerable overlap among the lists of responsibilities of the three bodies. The focus of the NBC is to establish national policies on biosafety; authorize commercial release of, and trade in, crops and products derived through biotechnology; ensure regulatory compliance; coordinate with trading partners on issues relating to biotech products; and provide information (except for Confidential Business information) to developers and the public. The function of the TAC is to provide the technical information needed by the NBC to effectively do its job; evaluate applications for field trial licenses and provide recommendations to the NBC regarding the issuance of licenses; and to monitor new technological developments to assess any associated biosafety risks. Institutional Biosafety Committees are responsible for day-to-day research activities within their institutions, including monitoring ongoing research projects and ensuring that required

62 See WTO Dispute 291 http://www.wto.org/english/tratop_e/dispu_e/cases_e/ds291_e.htm

63 From Section 2. Application., S.R.O. (I) 336(I)/2005.

64 Biosafety & Genetically Modified Organisms. 2007. National Biosafety Centre, Pakistan Environmental Protection Agency, Ministry of the Environment, Islamabad.

records are kept; inspecting lab facilities and containment measures; coordinating with NBC to provide guidance and training to researchers, and establishing institutional emergency response plans.[65]

The central regulatory mandate of the Biosafety Rules is that any commercial activity (import, export, sale, purchase, or trade), involving a living modified organism (LMO) or a product made from one, requires a license. Similarly, the deliberate release of an LMO into the environment, such that the organism is not contained, as in the case of a field trial, also requires a license. Contained use, meaning laboratory research performed inside a physical structure limiting the LMO's contact with the environment and the public, must also be licensed. The unintentional release of an LMO is always a violation of the rules.

The NBC issues licenses to conduct these regulated activities under authority granted through the National Environmental Protection Act. Specifically, the license is issued pursuant to section 14 of the Act, dealing with hazardous substances:

"…no person shall generate, collect, consign, transport, treat, dispose of, store, handle or import any hazardous substance except…under a license issued by a Federal Agency…."

The licensing process imposes an affirmative duty on the applicant to comply with the Biosafety Guidelines (discussed later in this paper), including the duty to report accidents that could lead to harmful releases. Also, applicants agree to submit to inspection by the NBC.

Licenses are renewable in two-year increments, but may be revoked by the NBC under three circumstances: (1) if new evidence is found demonstrating harmful effects of the genetically engineered organism covered by the license; (2) if the genetically engineered organism causes unexpected environmental or health injury; or (3) if the license holder is not in compliance with any Federal requirements or conditions. Applicants whose license applications are denied may reapply, after six months, if they present new information relative to the environmental risk of the organism.

The Rules single out imports and exports for additional requirements. Trans-boundary movement of LMOs, whether for field trials or for food, feed, or processing, must be done in accordance with Article 18 of the Cartagena Protocol.[66] Essentially, this provision requires the LMO be properly identified as to the genetically engineered traits and any special handling necessary. For exports, the exporter must supply all risk assessment information and field trial data to the importing country. In addition, all trans-boundary movements must be done in accordance with the National Plant Quarantine Regulations to prevent the introduction of agricultural pests.

NATIONAL BIOSAFETY GUIDELINES

The National Biosafety Guidelines (the Guidelines) were finalized in May 2005, by the Pakistan Environmental Protection Agency (Pakistan EPA), following a multi-stakeholder consultation process including representatives from academia, research and development centers, industry, and non-governmental organizations. The purpose of the Guidelines was to provide guidance for conducting laboratory and field research using GMOs and for the commercial release of GMOs, as well as to establish regulatory processes consistent with the Pakistan Biosafety Rules (the Rules). The Guidelines also include the forms necessary for the implementation of these processes, along with instructions for completing the forms. In addition, the Guidelines clarify the roles played by the three authorities responsible for the regulation of biotechnology: the Institutional Biosafety Committees (IBCs), the Technical Advisory Committee (TAC), and the National Biosafety Committee (NBC).

In Chapter 1, the Guidelines present an extensive and largely positive discussion as to the nature of biotechnology and the valuable products that have been developed using this technology. However, this discussion is counterbalanced by a list of biological, environmental, and socioeconomic 'concerns':

1. Changes in ecological roles
2. Changes in genetic relationships
3. Changes in allergenicity, toxicity, or nutritional composition of foods
4. Indirect effects
5. Ethical and social issues

65 Large institutions or those with many diverse biotech research programs may also appoint Biosafety Offices at the program or lab level to facilitate coordination with the IBC and assist in the preparation of lab-specific standard operating procedures.

66 The relevant portion is paragraph 2(a)-(c):

(a) Living modified organisms that are intended for direct use as food or feed, or for processing, clearly identifies that they 'may contain' living modified organisms and are not intended for intentional introduction into the environment, as well as a contact point for further information. The Conference of the Parties serving as the meeting of the Parties to this Protocol shall take a decision on the detailed requirements for this purpose, including specification of their identity and any unique identification, no later than two years after the date of entry into force of this Protocol;

(b) Living modified organisms that are destined for contained use clearly identifies them as living modified organisms; and specifies any requirements for the safe handling, storage, transport and use, the contact point for further information, including the name and address of the individual and institution to whom the living modified organisms are consigned; and

(c) Living modified organisms that are intended for intentional introduction into the environment of the Party of import and any other living modified organisms within the scope of the Protocol, clearly identifies them as living modified organisms; specifies the identity and relevant traits and/or characteristics, any requirements for the safe handling, storage, transport and use, the contact point for further information and, as appropriate, the name and address of the importer and exporter; and contains a declaration that the movement is in conformity with the requirements of this Protocol applicable to the exporter.

In light of these concerns, the Pakistan EPA concluded that a national biotechnology policy, with appropriate safety protocols, would ensure environmental and human safety, without being so stringent that research efforts were impaired. In Pakistan EPA's opinion, the Guidelines would also promote biotech research and development efforts and enable collaborative projects with foreign scientists.

The processes established by the Guidelines anticipate nine different activities described by a matrix. One coordinate of the matrix is the type of work proposed: laboratory work, field work, and commercial releases. The other coordinate is the level of anticipated risk: minimal, low, and considerable. Each locus in the matrix could be associated with a set of requirements, processes, and forms.

Chapter 2 covers the portion of the matrix dealing with laboratory research (See Table 5), describing how the Principal Investigator should interact with the IBC.

Table 5. Laboratory research activities performed in different risk categories†.

Risk Category	Laboratory Work Undertaken
1—Minimal	• Tests with microorganisms that naturally exchange genetic material (pathogens are allowed) • Fusion of protoplasts of non-pathogenic microorganisms or plant protoplasts • Fusion of animal cells that does not result in a viable organism
2 —Low	• Tests with host/vector systems • Genetic engineering of whole plants • Work with animals, animal cells, zygotes or embryos resulting in a novel organism
3 —Considerable	• Work with genetic material known to cause disease • Alteration of a pathogen's host range • Work with genetic material known to produce human growth regulators or toxins • Work with virus production using animals • Propagation through 'cloning' (assumed to mean animal cloning) • Work with 'uncharacterized materials'

† Chapter 6 provides additional detail regarding laboratory work that poses specific hazards. These hazards include work with hazardous gene products, viral vectors, and animals infected with viruses.

All proposals for laboratory work are sent to the IBC for consideration, and the IBC may request any additional information from the proponent that it deems necessary. The IBC confirms the Risk Category, and if Risk Category 1 or 2 applies, work may begin once the IBC gives its approval. Records involving Risk Category 2 and 3 proposals must be forwarded by the IBC to the NBC, via the TAC. If the IBC determines that the proposed work is appropriately placed in Risk Category 3, consent must be obtained from NBC and the IBC, before work may commence.

Conditions for laboratory work are determined on a case-by-case basis, but generally, as the perceived risk increases, the IBC will require more secure levels of containment and additional training for laboratory personnel. The initial determination of risk category by the IBC may be adjusted up or down, in light of new information.

Chapter 3 of the Guidelines covers Field Work, but the chapter does not explicitly designate the risk category for a particular research proposal. Risk category 1 activities can be inferred for microorganisms and plants, but there is no guidance for categories 2 or 3. For animals, there is little guidance regarding appropriate risk categories.[67] (See Table 6)

Table 6. Field work activities performed in different risk categories.

Risk Category	Field Work Undertaken
1—Minimal	• Microorganisms with a history of safe use in the field or microorganisms that are similar to previously field-tested microorganisms • Plants modified through conventional breeding methods (selective breeding, mutagenesis, protoplast fusion, embryo rescue) • GM plants with familiar, non-hazardous traits
2 —Low	• Work with live animals, fertilized oocytes, or embryos resulting in a novel organism

Overall, the impression given by Chapters 2 and 3 is that the IBC has considerable latitude in determining the risk category for a given research proposal, and this latitude is echoed in the brief Chapter 4, which describes containment conditions for field trials. For organisms with a history of prior field work, the only requirement is that the control and containment of the work complies with relevant regulations. However, for untested microorganisms and plants, there are lists of specific measures that must be observed. These measures are analogous to those required in other countries, such as proper signage, restricted access, site inspections by regulatory staff, and destruction of test organisms at the completion of work.[68] For field work with animals, conditions are determined on a case-by-case basis.[69]

Chapter 5 begins with a reiteration of the composition and responsibilities of the three regulatory bodies (NBC, TAC, and IBC) and the Bio-safety Officer, as reflected in the Rules. The Guidelines emphasize the need for worker training and emergency preparedness procedures. It is even suggested that workers engaged in microbiological experiments have serum samples taken regularly to monitor inadvertent exposure to the test organisms. The Project Supervisor[70] is designated as the individual responsible for providing the IBC with all necessary

67 However, Chapters 4 and 6 provide some guidance for field trials of animals.

68 Chapter 6 provides greater detail regarding confinement conditions for Risk Category 2 and 3 field trials of GE plants, such as isolation distances, pollen traps, and post-trial monitoring for volunteers. An unusual requirement is that soil samples be collected to verify that no viable plant tissue is left in the field after trial completion.

69 Chapter 6 provides additional guidance regarding research on transgenic animals.

70 Used interchangeably with 'Principal Investigator'.

information and for carrying out the field work in compliance with the applicable regulations, including notifying the IBC in the event of an accident.

The movement of experimental organisms is handled in Chapter 7. Double containers are required for the movement of all regulated materials, but specific container types are not discussed, leaving it to the discretion of the IBC and Project Supervisor to select appropriate containers. Researchers who are shipping experimental organisms or products thereof to colleagues in Pakistan and abroad must first consult with the IBC. The recipient must be provided with a full characterization of the organism and its inherent risks, and notice must be given to the Biosafety Officer, IBC or other appropriate authority at the recipient's institution.

Chapter 9 summarizes the regulatory process itself. Once an initial proposal to perform regulated work is received by the IBC, the project proponent will be informed as to the status of the project within thirty days. If the proposal must be passed up to the TAC, because of the risk category, the TAC has an additional thirty days to review the proposal before sending it to the NBC. For 'high-risk'[71] projects, the NBC may take up to three months to respond to the proponent. If a response is not received from the appropriate regulatory body by the designated deadline, the proponent may assume approval and proceed with the work.

Chapter 10 presents the forms associated with a proposal to perform laboratory work. The project proposal form solicits information regarding the objectives of the research project, the biology of the test organism, and the confinement measures to be used. Additional questions must be answered if the test organism is a plant or an animal. The IBC proposal assessment form allows the IBC to indicate its decision regarding the Risk Category applying to the proposal and its determination as to whether the application has provided adequate answers to all questions. The IBC may also indicate on the form any additional conditions that must be met by the applicant.

Chapter 11 presents the forms associated with a proposal to conduct a field trial. The application form asks for basic information regarding the nature of the experiment and the test organism, as well as the confinement measures to be used, but the form asks for additional details via a set of 'Core Questions', the answers to which may be considered as the application form is completed.

Unfortunately, these questions venture beyond what is useful for consideration of a confined field trial. For example, core question 11.1.8.E asks if the organism is to be consumed as food. It must be assumed that the regulators are not asking if the organism produced *in this field trial* will be used as food, but rather, if someday, organisms derived from the test organisms would be consumed. Follow up questions on nutritional composition, processing, and the presence of the organism in food products are not relevant to establishing confinement and are likely to present an undue burden for a researcher attempting to perform a small field trial.

The 'Additional Points' to consider regarding a field trial of a GE plant also includes questions which may be problematic or even impossible for the proponent to answer at the time of application. A sample is presented here:

- Will the plants be allowed to set seed in *future experiments*?
- What farming systems would use the commercialized version of the test organism?
- How would an herbicide-tolerant GE plant impact herbicide usage/weed control/use of environmentally friendly chemicals?
- What Integrated Pest Management strategies would be used on the commercialized version of the plant?

The form also asks for information a *priori* that will not be available until *after* the field tests are completed:

- Pleiotropic effects
- Competitiveness in unmanaged ecosystems
- Adverse consequences
- Secondary ecological effects on other species

Similar questions are posed for other organism, and while many of the questions posed in Chapter 11 are presented as 'things to consider', it is unclear how answers, or the lack of answers, will be treated within the regulatory system. Further, there is some confusion regarding the appropriate information related to each stage of product development (i.e., laboratory, greenhouse, field trial, environmental release) which may lead to difficulty in obtaining permission to conduct experiments.

Chapter 11 also includes the form to be used by the IBC to assess the field trial proposal. It is interesting that the form does not ask for the IBC's opinion on the proponent's answers to the 'Core Questions' or the 'Additional Points'. Instead there is a single question (#12—IBC assessment), which asks for an evaluation of the project, the project supervisor's capability to manage the work, and the adequacy of the project design, site selection, and contingency plan.

The process for commercializing genetically engineered organisms is covered in Chapter 12. The process is initiated by an applicant, who must provide sufficient data to the NBC in support of the application. The data requested are typical of commercialization processes in other jurisdictions and include crop biology, transformation method, molecular characterization, protein expression, and agronomic performance (including disease susceptibility), and toxin production. It is encouraging that the dossier may include data collected from field trials outside Pakistan as well as data regarding similar products.

71 Chapter 9 uses the terms 'low', 'medium', and 'high' risk, rather than 'minimal', 'low', and 'considerable' risk, used earlier in the Guidelines.

However, the process seems to establish an impossibly high and unscientific hurdle to surpass, namely that the proponent 'show that the experimental organism and its products are free from any risk'. Although it is possible for data to show that risks posed by commercialization are extremely unlikely or that the amount of risk posed is extremely small, it is generally accepted that no amount of experimentation and data can prove a total absence of risk. Given that the National Biosafety Committee has allowed the commercialization of Bt cotton, it is likely that, in practice, the NBC looks to see if commercialization will result in *significant* risks and that any risks posed can be mitigated.

As for the nature of the risks themselves, the Guidelines do not provide a list of resources to be protected from adverse impacts, a fundamental early step in environmental risk assessment. Instructions accompanying the application form indicate that the government is concerned with crop weediness, decreases in pest resistance, and adverse impacts to non-target organisms and beneficial insects.

Lastly, in Chapter 13 the Guidelines allow lab work and field work with specific genetically modified organisms to be granted 'Exempt Status', if such work would have 'no risk'. As with applications for commercialization, there is no guidance as to what 'no risk' means or how it is to be demonstrated: the proponent must simply provide reasons why the lab or field work merits an exemption. The application is filed with the IBC, but it is unclear which regulatory body has the authority to grant exempt status. In Chapter 13, the decision is said to be made by the IBC, and in section 2.1.2 of the Guidelines, the IBC is said to make the 'final decision' on exempt status. But in the Executive Summary of the Guidelines, the IBC is said to make recommendations to the NBC regarding exempt status.

The Guidelines conclude with twelve appendices, the first eleven of which provide advice to researchers involved in genetic engineering research.

- Appendix 1 provides a list of selected 'Good Laboratory Practices'. The list is not comprehensive: the focus is on minimizing contact with experimental microorganisms.
- Appendix 2 lists specific vectors that are authorized by the National Biosafety Committee to be used with bacterial, fungal, plant, and mammalian host species. The host/vector combinations were chosen on the basis of low potential for survival outside the laboratory environment. In addition, this appendix addresses the use of electroporation and other means of cell transformation that do not involve biological vectors. Such non-biological methods are approved for use if the gene donor organism does not cause a plant or animal disease and if the donor DNA does not comprise more than 2/3 of a complete viral genome or result in the production of a toxin or mammalian growth regulator.
- Appendix 3 lists highly toxic substances, the use of which in research constitutes Risk Category 3 work, as described in Chapter 2.
- Appendices 4, 5, and 6 provide the requirements for Containment Level C1, C2, and C3 respectively. The list of Level C1 measures is based on Good Laboratory Practice, but provides greater detail than Appendix 1. Level C2 includes all provisions laid out in Level C1 and requires additional measures to protect personnel and ensure that research organisms do not escape the laboratory. Level C3 is the highest containment level, including measures from Level C2, plus any additional measures, determined by the National Biosafety Committee on a case-by-case basis.
- Appendices 7, 8, and 9 provide the requirements for the operation of Plant Glass Houses at Biosafety Level PH1, PH2, and PH3 respectively. As for laboratory containment, the higher containment levels include the measures employed at the lower levels. Although an existing greenhouse could theoretically be retrofitted to meet the requirements for a PH1 or PH2 glass house, a greenhouse meeting PH3 requirements would likely need to be custom constructed. A PH3 greenhouse would have to be built airtight, because it must always operate under negative pressure, and any air flow, either into the house or exhausted from the house, must pass through a HEPA filter. Given that greenhouses normally are constructed with thousands of joints between the frame and the glazing material, this single requirement would make the cost of construction prohibitive.
- Appendices 10 and 11 provide the requirements for the operation of Animal Houses at Biosafety Level C1A and C2A respectively. As with PH3 greenhouses, a C2A facility must also operate continually at negative pressure.

Lastly, Appendix 12 provides the glossary for the Guidelines. It provides definitions for technical terms used in the Guidelines as well as terms that do not appear in the Guidelines but are routinely used in the field of biotechnology.

CHALLENGES FACING THE BIOSAFETY REGULATORY SYSTEM IN PAKISTAN

ADMINISTRATIVE EXPERIENCE (PRIOR TO APRIL 2010)

The Biosafety Rules 2005 and the Biosafety Guidelines 2005 provide the foundation for a national biosafety regulatory system in Pakistan. However, significant challenges remained with respect to building functional capacity, transparency and predictability of regulatory processes. The National Biosafety Committee (NBC) and the Technical Advisory Committee (TAC) were assembled and meetings of both groups were held regularly, at least until August of 2010.[72] A National Biosafety Centre was established at Pakistan Environmental Protection Agency (Pak EPA) to serve as a secretariat for the NBC and TAC and handle administrative functions related to biosafe-

72 USDA FAS GAIN Report: Pakistan, Biotechnology (8/2/2010).

ty. This arrangement would seem to be advantageous because the Director General of Pak EPA is the mandated chair of the TAC and serves as the mandated Secretary for the NBC while the Director of Pak EPA is the mandated Secretary of the TAC. However, the Centre was funded as a special project and concerns about the lifespan of the Centre and continued funding limited its effectiveness, particularly in terms of the ability to build internal capacity and to provide administrative leadership within the biosafety regulatory system.

REGULATORY REVIEW OF BT COTTON

As discussed earlier in this analysis, the experience in Pakistan with commercial release of GE plants is limited to Bt cotton and this illustrates many of the challenges faced by the regulatory system. Transgenic Bt cotton arrived in Pakistan well before the establishment of the Pakistan Biosafety Rules in 2005. Research collaborations with Monsanto as early as 1998[73] along with 'unregistered' imports from India provided material for local seed suppliers to use. By 2005 much of the cotton planted in Pakistan was Bt. By the time of the first approvals in 2010, nearly all of the cotton in Pakistan was Bt.[74]

The presence of large amounts of unregulated material posed unique problems for the nascent regulatory system, many of which were unrelated to biosafety. Questions surrounding intellectual property and plant breeders' rights delayed the entry of any Bt cotton varieties into the regulatory system but not into farmers' fields. Further, the proliferation of local varieties presented a challenge. When the Province of Punjab formed a committee to plan for the short term commercial and regulatory development of Bt cotton in 2008, 8 varieties were chosen to submit to the NBC from 39 identified by the PARC. These varieties were eventually approved in March 2010 following the granting of an exemption from additional biosafety studies by the NBC.[75]

Although this is generally considered a regulatory success, it again highlights challenges facing the biosafety regulatory system. First, regulation of transgenic plants at the variety level will require duplicative and burdensome regulatory reviews for plant and gene construct combinations that have previously been demonstrated to be safe in the environment. Most regulatory systems for biosafety regulate at the level of transformation event – with subsequent varieties developed through breeding programs not requiring additional biosafety review. Second, the decision and deliberations for the approval of Bt cotton varieties was not a transparent regulatory process. Even today it is difficult to identify precisely which varieties have received approval and documentation of the decision is not readily available to the public or obtainable through request. Coupled with the wide scale cultivation of Bt cotton varieties prior to any approvals, this does not engender public confidence in the regulatory process. The lack of concerted communication from regulatory authorities has contributed to an information deficit that is frequently filled with spurious information from interest groups and activists that is reported in the media.

EXTERNALITIES

The Biosafety Regulatory System in Pakistan has also been challenged by a number of externalities that have nothing to do with biosafety or risk assessment for transgenic plants. While many of these externalities are not unique to Pakistan they contribute to the difficulties in implementing an effective biosafety system. They include the lack of a well-developed professional seed industry; lack of consistent funding and infrastructure for agricultural research; and lack of intellectual property protection, especially for plant breeders. Because of other pressing domestic policy and security concerns, it may difficult to focus attention on biosafety regulation, especially given the experience with Bt cotton. As elsewhere, the role of multinational companies in agricultural production systems has been conflated with issues related to biosafety.

DEVOLUTION OF FEDERAL AUTHORITIES

In April of 2010, the 18th Amendment to the constitution of Pakistan was passed by the National Assembly. The amendment was intended to curtail presidential power and to provide more autonomy to provincial governments. As part of this process, 17 federal ministries were devolved, with their authority reverting to provincial government. Among the 17 ministries devolved were the Ministry of Education, Ministry of Environment, Ministry of Food and Agriculture, and the Ministry of Health. Each of these provided members to the NBC and in fact only the Ministry of Science and Technology remains in existence of the original 5 ministries with mandated membership in the NBC.

Understandably, the reorganization associated with devolution created confusion and difficulty for the biosafety regulatory commission. Although the Ministry of Environment was devolved, Pak EPA remains in existence and was first transferred into the Capital Administration and Development Division (CAD). Subsequently, the agency was moved to the Ministry of National Disaster Management and is now located within the Ministry of Climate Change. It remains to be seen if this will be permanent and how it will ultimately affect the National Biosafety Centre, which still operates within Pak EPA.

73 The collaboration collapsed due to change of government in 1999, but the Bt material remained in Pakistan and was used for development of local varieties. (Personal communication, Punjab Department of Agriculture.)

74 USDA FAS GAIN Report: Pakistan, Biotechnology (8/2/2010).

75 Personal communication, Punjab Department of Agriculture.

CHALLENGES AND OPPORTUNITIES

When the devolution of federal ministries was completed in summer 2011, it was unclear how the biosafety regulatory system would continue to function. At present, it appears that the NBC is being reconstituted to replace ministry personnel and to ensure continued adequate representation from the provincial authorities to account for their greater authority over agricultural and environmental management.[76] It remains to be seen how the Provincial authorities will respond when the NBC issues a decision.

In conjunction with the reorganization that has been mandated by the 18th amendment, there is a unique opportunity to evaluate and clarify elements of the biosafety framework.

IMPROVING TRANSPARENCY

'Transparency' in terms of regulatory processes does not have an established and widely accepted definition, but it generally refers to the ability of stakeholders to understand how a process is intended to work and how it is operating in practice related to a given decision or regulatory action. First and foremost, transparency increases stakeholder confidence that regulatory processes are functioning as intended, and allows the opportunity to identify if they are not (i.e., provides accountability). In this context, stakeholders can include the general public but also regulated industry, politicians and importantly in the case of Pakistan, provincial governments. If stakeholders are confident that a defined and acceptable regulatory process is being followed, confidence in decisions will rise. Transparency also affords the opportunity to get feedback from stakeholders on how the process can be improved. Transparent regulatory processes also improve perception that decisions being made are legitimate and decrease the perception of corruption.

At present, the regulatory process for biosafety in Pakistan is opaque. Although the Biosafety Rules and Biosafety Guidelines lay out a regulatory process, it is difficult to ascertain what decisions are being made and it is difficult or impossible to find authoritative documentation of those decisions. Further, it is not clear what processes and procedures are being followed in order to inform and generate decisions. This lack of transparency undermines regulatory decision making and increases the controversy surrounding decisions.

A number of steps could be taken to improve the transparency of the biosafety regulatory process in Pakistan. First, the dissemination of decisions and associated technical documentation could be made publicly available. This could be done using a combination of resources such a website, e-mail list, publication in the national gazette, distribution of physical publications or even just establishing a process where information could be provided by request. The obvious organ of government for managing the dissemination of information related to biosafety appears to be the National Biosafety Centre at Pak EPA, although it is unclear if that group has the financial and human resources to carry out this function.

PREDICTABILITY

Predictable regulatory processes are advantageous because they allow stakeholders (including the public, regulated industry and political officials) to know both when decisions are likely to be made, along with knowing how decisions will be made (i.e., what information will be considered). Predictability is valued by regulated industries because it allows for more accurate and reliable financial planning, but it is also an important component of transparency which engenders public trust. In addition to the steps described above, predictability in the Pakistan biosafety regulations could be fostered by the elaboration of processes and procedures through guidance describing what sort of data will be considered when looking at environmental risks associated with the release of GE plants. Guidance which elaborates and explains the regulatory process could also be provided, including guidance on the operation and requirements for Institutional Biosafety Committees (IBCs). The IBCs operate reasonably independently and a set of SOPs for conducting their work would serve to provide reassurance that they are adequately performing their role in oversight of research. This would also ensure that proposals and recommendations forwarded to the NBC and TAC could be expected to be relatively uniform and of acceptable quality. Another step to improve predictability is to establish, well in advance, a schedule for meetings and deliberation of the NBC and TAC. This would allow applicants to understand in advance the timing of their submissions and when they can expect decisions.

TECHNICAL AND REGULATORY CAPACITY BUILDING

Even prior to devolution, there was a need to build technical and regulatory capacity within the Pakistan Biosafety Framework. The reorganization caused by implementation of the 18th amendment provides an opportunity to identify technical and regulatory needs and to integrate a program of capacity building into the biosafety regulatory system. It also provides a motivation to make sure that stakeholders, including Provincial governments understand the system and are invested in its success.

Pakistan has several advantages for building technical and regulatory capacity. Chief among these for the purpose of biosafety regulation is the presence of Ph.D. level researchers who have received training domestically and internationally in related areas of agricultural research and development. These scientists can be tapped to fill positions on the NBC and TAC and to provide ad hoc support when their expertise is relevant to deliberations in these bodies. The challenge for capacity building is establishing a clear understanding of how biosafety

76 Personal communication, Ms. Nazia Batool, Pak EPA.

regulation differs from research under the relevant disciplines that inform environmental risk assessment, and what the scope of regulation will be.

CONCLUSIONS

Biosafety Regulation in Pakistan faces many daunting challenges, including broad social and political disruption, poorly funded agricultural research infrastructure, difficulty in enforcement of existing and related regulations and the conflation of biosafety with other agricultural and socio-political concerns. However, there is a pressing need for a functional biosafety system in order to allow the development of beneficial agricultural technologies to meet the countries long term agricultural development needs. The foundation for regulation is laid out in the Pakistan Environmental Protection Act (PEPA) and elaborated in the Biosafety Rules 2005, and the associated Biosafety Guidelines. In order to improve functional capacity for biosafety regulation improved transparency for the regulatory process and an enhanced understanding of the nature of biosafety as a scientific and regulatory construct will be required.

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