Some Imperatives and Challenges for Rice Biotechnology in Asian National Agricultural Research and Extension Systems

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Rice in Asia

Rice, *Oryza sativa L.*, is the staple food for more than three billion people or over half the world's population (FAO 2004). It provides 27 per cent of the dietary energy supply and 20 per cent of dietary protein intake in the developing world. Grown in at least 114 mostly developing countries, rice is the dominant crop in Asia where it covers half of the arable land used for agriculture in many countries (Cantrell and Hettel 2004). Moreover, it is the primary source of income and employment for more than 100 million households in Asia and Africa (FAO 2004). The Asian continent, where 56 per cent of humanity including 70 per cent of the world's 1.3 billion poor people lives, produces and consumes around 92 per cent of the world's rice (Papademetriou 1999). Over 50 per cent of the 840 million people suffering from chronic hunger live in areas dependent on rice production. About 80 per cent of the world's rice is produced in small farms, primarily to meet family needs, and poor rural farmers account for 80 per cent of all rice producers (FAO 2004). Nine of the top ten rice producing countries in 2003, viz., China,

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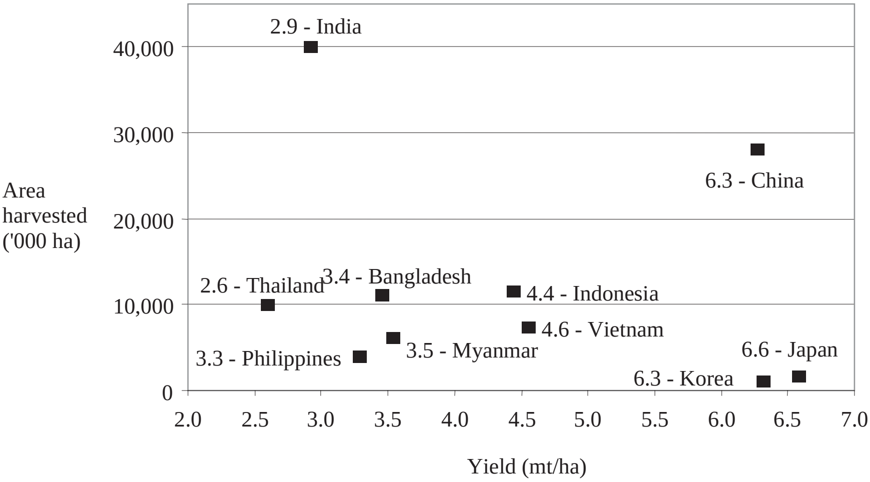
India, Indonesia, Bangladesh, Vietnam, Thailand, Myanmar, the Philippines, and Japan are in Asia. China and India combined account for more than half of the world's rice area and, along with Indonesia, consume more than three-fourths of the global rice production (Hossain 1997; Maclean *et al.* 2002). However, less than seven per cent of the world's rice production is traded internationally (Maclean *et al.* 2002) and, with this small marketable surplus, prices fluctuate widely with droughts, floods, and typhoons (Hossain 1997).

But more to being the world's most popular staple, rice has been cultivated by mankind for more than 10,000 years. Hence, it provides a symbol of global unity and cultural identity for many countries where rice cultivation is practically intertwined with religious observances, festivals, customs, folklore, and traditions. The United Nations, therefore, declared 2004 as the International Year of Rice, with a theme that captures the meaning of rice to so many peoples and cultures: Rice is Life.

The Challenge to Increase Rice Productivity

The Green Revolution beginning in the 1960s ushered in an era of high rice productivity, with yields doubling or tripling from 1.9 tonnes per hectare (t/ha) in many Asian countries (Figure 1). Between 1966 and 2000, the rice production growth of 130 per cent, from 257 million

Figure 1: Area harvested and yield levels (mt/ha) in major Asian rice-growing countries (FAO, 2003)



tonnes in 1966 to 600 million tonnes in 2000, outpaced the population growth of 90 per cent in low income countries. The average per capita food availability was 18 per cent higher in 2000 than in 1966 (Khush 2004). About 84 per cent of rice production growth has been attributed to the use of modern technologies such as rice varieties that are semi-dwarf, early maturing, non-photoperiod sensitive and can, therefore, be planted more than once a year, and responsive to nitrogen fertilizer (Maclean *et al.* 2002). More than 2,000 modern varieties, with resistance and tolerance to biotic and abiotic stresses, have been commercially released in 12 countries of South and Southeast Asia over the last 40 years (Cantrell and Hettel 2004). As a consequence, rice production cost per unit output was reduced by 20-30 per cent. This translated to reduced rice prices at the consumer level from about US$450 per metric tonne (mt) unmilled rice in the early 1950s to less than US$300 per mt by 1999 (Maclean *et al.* 2002), with world market rice prices decreasing by 80 per cent over the last 20 years (Cantrell and Hettel 2004).

In Asia, however, demand for rice is projected to increase by 70 per cent over the next 30 years, driven primarily by population growth that, excluding China, is expected to increase by 51 per cent (Hossain 1997). It is estimated that the Asian population will increase from 3.7 billion in 2000 to 4.6 billion in 2025 (Cantrell and Hettel 2004). In the Philippines, for example, the population is expected to reach 107 million by 2025 and 65 per cent more rice, relative to present levels, would need to be produced to keep up with demand by a population continually growing by 2.3 per cent each year. This translates to a required sustained year on year rice production growth of 3 per cent. Given that annual rice production growth rates have been decelerating to less than 2 per cent per year, and the land frontier, the primary source of growth in recent years is closing, major technological progress has to be achieved in the next two decades to avoid importation. Against a backdrop of decreasing land, labour, and water and rising prices of production inputs, the challenge to further increase rice productivity is indeed enormous.

Constraints in Asian Rice Production

Rice production and post-production processes in Asia are severely compromised by pests, diseases, and physiological and environmental factors. The rice crop, for example, is the world's single largest market for agrochemicals, consuming around US$3.7 billion annually, with agrochemical costs and crop losses amounting US$ tens of billions per year (DFID 2004). Tungro, the most destructive viral disease in Southeast Asia, for example, results in crop losses worth more than US $1.8 billion annually (DFID 2004). Moreover, rice cultivation per se is restrained by resource constraints, among the most important of which are the projected scarcity of water (Tuong and Bouman 2002) and scarcity of land. Technological progress is required to increase crop water productivity of rice (Cantrell and Hettel 2004) and rice crop productivity under fragile environments such as the rainfed lowlands and uplands.

Biophysical constraints account for substantial yield losses in Asia (Hossain 1997, Evenson *et al.* 1996) (Table 1). In the irrigated ecosystem, yield loss due to technical constraints accounted for 20 per cent (962 kg/ha) of the average yield, with soil-related problems being the most significant. On the other hand, yield loss due to technical constraints accounted for 33 per cent of average yield in the rainfed lowland and flood-prone ecosystems, with submergence being the most important, while it was more than 40 per cent of the average yield in the upland ecosystem, with drought being the most significant. Overall, all technical constraints caused a total yield loss of about 23 per cent or 833 kg/ha in Asia, with abiotic constraints being more important than biotic constraints for all ecosystems. Climate-related constraints like submergence, drought, and cold resulted in yield losses that ranged from 227 kg/ha (20 per cent of average yield) for the upland to 429 kg/ha (28 per cent of average yield) for the flood-prone ecosystems. Yield losses due to pests and diseases, on the other hand, were most significant in the rainfed ecosystem while, that due to weeds were most important for the upland environment.

The Role for Rice Biotechnology

Agricultural biotechnology in Asia has been recognized as having the potential to: (i) increase crop and animal productivity; (ii) improve nutritional quality; (iii) broaden tolerance of crops for drought, salinity, and other abiotic stresses; and (iv) increase resistance of crops to pests and diseases (ADB 2001). In the case of rice biotechnology, the Rockefeller Foundation (RF), in the process of developing its International Programme on Rice Biotechnology or IPRB (Evenson *et al.* 1996, O'Toole *et al.* 2001), identified the top-20 priority traits for biotechnology research intervention, balancing research costs vis a vis the benefits from expected increases in rice productivity or value.

Table 1. Yield loss due to technical constraints in the rice ecosystems of Asia (Evenson et al 1996).

Constraints	Irrigated (kg/ha)	Rainfed lowland (kg/ha)	Flood-prone (kg/ha)	(kg/ha)	Average for AsiaLoss	
					Upland (kg/ha)	Loss (%)
Biotic						
Diseases	69	146	18	70	83	3.1
Insects	108	166	16	65	110	2.3
Other pests	29	88	21	120	52	1.4
Abiotic						
Water	400	288	429	227	358	9.9
Soil	356	75	13	80	229	6.4
Total	962	763	496	563	833	23.1
Loss as % of yield	19.6	33.2	33.1	40.2	23.1	

Guided by this prioritization, the RF in the mid-1980s supported a 17-year programme that laid the scientific foundation for 'rice biotechnology' as we know it to-day. At about the same time, Asian national agricultural research and extension systems (NARES) began building biotechnology capacity. Among the important accomplishments of the IPRB were: (i) the generation of the first DNA molecular marker map of rice; (ii) the regeneration and transformation of rice; (iii) the use of rice pest genomic information to understand host-plant resistance; (iv) discoveries that changed the way rice geneticists viewed breeding objectives such as insect resistance, abiotic stress tolerance, and hybrid rice; (v) the discovery of rice's pivotal genomic position in the evolution of cereal species; (vi) the transfer of the resulting biotechnologies to institutions in rice-producing and -consuming countries; and (vii) the strengthening of both physical and human resources in cooperation with national and international rice research systems in Asia, Africa, and Latin America (O' Toole *et al.* 2001). The latter involved international collaborative research-cum-training that successfully linked emerging national rice biotechnology efforts directly to advanced research institutes in the United States, Europe, Japan, and Australia, resulting in the training of more than 400 rice scientists, primarily from Asia, in advanced laboratories around the world. At least 73 institutions in 12 Asian countries received both research grants while having up to 20 of their scientists sent to formal training activities that included: (i) Ph.D. fellowships; (ii) dissertation fellowships; (iii) postdoctoral fellowships; (iv) visiting scientist fellowships; (v) biotechnology career fellowships; and (vi) technology transfer fellowships in advanced laboratories and universities in developed countries (O' Toole *et al.* 2001).

Beginning 1993, the Asian Rice Biotechnology Network (ARBN) was also formed, with IRRI as coordinator, and this facilitated research collaborations amongst several Asian rice breeding programmes with a primary objective of developing disease resistant varieties through the application of DNA marker technology (Leung *et al.* 2004). Among the major Asian R&D institutions involved in the ARBN were the Indonesian Agricultural Biotechnology and Genetic Resources Institute, the Central Rice Research Institute in India, the Punjab Agricultural University also in India, the Philippine Rice Research Institute (PhilRice), the Agricultural Genetics Institute in Vietnam, and the China National Rice Research Institute (CNRRI).

Progress in Rice Biotechnology Applications

With increased activities on rice biotechnology beginning in the mid-1980s, rice gradually became the 'model monocot plant' in molecular genomics research, eventually becoming the first food crop for which complete genome sequence became available. Progress achieved in the application of biotechnology for rice improvement has been in two major areas-the use of molecular markers for identifying and incorporating favourable genes within the rice species, and the use of transgenic technologies to incorporate traits for herbicide tolerance, biotic stress resistance, abiotic stress resistance, and nutritional value into rice (Coffman *et al.* 2004, Leung *et al.* 2004).

Use of molecular markers. The development of the first rice molecular map in the late 1980s (McCouch *et al.* 1988) sped up molecular genetics research in rice. Among the early molecular marker applications for rice improvement were the: (i) construction of dense genetic maps using different populations; (ii) tagging and/or introgression of major genes and those underlying quantitative traits, referred to as quantitative trait loci (QTL); (iii) high-resolution characterization and fingerprinting of germplasm; (iv) assessment of the diversity of germplasm pools; and (v) map-based gene cloning. Molecular markers offered great potential for increasing the precision and speed of rice breeding as, among other advantages over phenotypic markers, they provided the ability to (i) screen breeding populations regardless of growth stage; (ii) screen for traits that were extremely difficult, expensive, or time consuming to score phenotypically; and (iii) distinguish the heterozygous condition without need for progeny testing (Coffman *et al.* 2004). Molecular markers provided geneticists with powerful tools to dissect the inheritance of economically important traits in rice, many of which are quantitatively inherited and complex in nature. Thus, studies dealing with QTL were carried out such as those involving tolerance to a variety of environmental stresses including drought, seedling vigour, submergence, salinity, and mineral deficiencies or toxicities (Champoux *et al.* 1995, Price *et al.* 2002, Redoña and Mackill 1996, Xu and Mackill 1996, Flowers *et al.* 2000, Gregorio 2002). These traits were considered primary targets for molecular marker-aided selection (MAS) as breeding for them using conventional techniques often proved to be difficult.

MAS or the selection of traits based on the presence or absence of a molecular marker or markers in lieu of phenotype has already received a lot of emphasis in rice. The development of simple and less costly marker systems based on the polymerase chain reaction (PCR) such as the simple sequence repeats or SSRs (McCouch *et al.* 2002) contributed greatly to the use of MAS in various laboratories in developing countries. For example, at PhilRice, the NARES for rice in the Philippines, MAS studies are conducted to develop varieties resistant to bacterial blight, including the pyramiding of two to three bacterial blight resistance genes in a common genetic background, both for inbred and hybrid rice breeding. Gene pyramiding is expected to provide durable resistance against rice insect pests and diseases and attempts in this direction have been tried early on for bacterial blight and rice blast diseases (Yoshimura *et al.* 1995, Hittalmani *et al.* 1995) and the insect brown planthopper (Su *et al.* 2002). Introgressing genes from wild relatives into cultivated rice has also been accomplished with the aid of molecular markers, such as the bacterial blight resistance gene from *O. longistaminata* (Ronald *et al.* 1992), and the yield traits from *O. rufipogon* (Thomson *et al.* 2003). Markers have also been used to minimize the linkage drag that occurs in wide crosses and to obtain the desired recombinants in fewer generations during backcrossing (Takeuchi *et al.* 2003, Blair *et al.* 2003). Whole-genome, marker-based selection allows for new opportunities to unravel and makes efficient use of genetic variation both in cultivated rice and its wild relatives.

One of the most significant developments aided by the use of molecular markers in rice was the map-based cloning of *Xa 21* and its subsequent use in developing varieties with broad spectrum resistance to bacterial blight (O'Toole *et al.* 2001). Starting with the genetic mapping using RFLP makers of the *Xa 21* locus in 1990 (Ronald *et al.* 1992), the gene was cloned using map-based cloning techniques and a bacterial artificial chromosome library by 1995 (Song *et al.* 1995, Wang *et al.* 1995). By 1997, the gene had been pyramided with other *Xa* genes using PCR-based MAS (Huang *et al.* 1997) and, by 1998, *Xa 21* had been transformed into elite lines (Zhang *et al.* 1998) with field trials conducted in China, India, and the Philippines by 1999 (Rockefeller Foundation, 1999). By 2000, a hybrid rice parental restorer line had been improved through MAS, resulting in resistant hybrid rices under field conditions (Chen *et al.* 2000).

The IRRI-coordinated Asian Rice Biotechnology Network that was supported by ADB and the RF played a key role in developing capacity for marker-aided analyses of pathogens and host plant resistance in several national breeding programmes. This network approach was found essential for the sharing of resources and providing sustained training in the adoption of new biotechnology tools and genetic knowledge in individual breeding programmes of different NARES in Asia (Leung *et al.* 2004). As a result of ARBN activities, elite or commercial rice lines with multiple disease resistance genes have been developed in several participating countries (Table 2).

Use of transgenic technologies. No genetically modified (GM) or transgenic rice has yet been commercialized in Asian countries. However, two GM rice, both involving herbicide tolerance, have already passed regulatory approval processes in the US: the Liberty-Link™ rice of Aventis Crop Science (now Bayer CropScience) involving phosphinothricin (PPT) herbicide tolerance, specifically glufosinate ammonium, and the CLEARFIELD™ rice involving imidazolinone herbicide tolerance from BASF Inc. (AgBios 2004). Ten trials in 11 hectares and 12 trials in 45 hectares were conducted in 2002 and early 2004, respectively, 90 per cent of which involved Monsanto (Jia *et al.* 2004). To indirectly gauge the extent to which the use of GM technology had so far advanced in rice, Coffman *et al.* 2004) utilized information on patent applications and classified these into the areas of: (i) herbicide tolerance; (ii) biotic stress resistance; (iii) abiotic stress resistance; and (iv) nutritional traits. Until 2002, 307 patents on rice biotechnology from 404 different groups had been filed (Brooks and Barfoot 2003). The largest number of patents was held by DuPont/Pioneer (68), followed by Monsanto (33), Syngenta (32), Bayer (19), public sector institutions in Japan, and Japan Tobacco.

Amongst various traits, herbicide tolerance has been the major focus for the private sector. In the US, Monsanto and Bayer were responsible for 80 per cent of GM rice field trials, primarily addressing herbicide tolerance (Brooks and Barfoot 2003). Other countries where herbicide tolerant GM rice has been field tested include Italy, Brazil, Argentina, and Japan, and possibly China (Coffman *et al.* 2004). Biotic stress resistance, on the other hand, has been the primary focus for public sector research institutions including those in Asia (Brooks and Barfoot 2003). Specific traits being worked on using GM technologies include resistance to bacterial blight using the gene *Xa*21, rice blast, rice hoja blanca virus, rice tungro spherical virus, rice yellow mottle virus, rice ragged stunt virus, the brown planthopper, and yellow stem borer, the latter, using *Bt* technologies, being the closest to commercialization. For abiotic stress tolerance, transgenic rice plants

Table 2. Marker aided selection (MAS)-improved varieties and their corresponding increase in yield developed by research teams from Asian NARES (Leung et al 2004)

Country	Background commercial/ Yield standard	Released (R) / Near-release (NR)	Yield (t/ha)	Gain over yield standard (%)
Philippines	IR64	AR32-19-3-2 (NR)	5.1	0
	IR64	AR32-19-3-3 (NR)	6.7	31.4
	IR64	AR32-19-3-4 (NR)	6.1	19.6
	BPI Ri10	AR32-4-3-1 (NR)	6.0	17.6
	BPI Ri10	AR32-4-58-2 (NR)	6.5	27.5
	PSB Rc28	Yield standard	5.1	-
Indonesia	IR64	Angke (Bio-1) (R)	5.4	20.0
	IR64	Conde (Bio-2) (R)	5.4	20.0
	IR64	Yield standard	4.5	-
India	PR106	IET17948 (PR106-P2) (NR)	8.2	22.4
	PR106	IET17949 (PR106-P9) (NR)	7.9	17.9
	PR106	Yield standard	6.7	-
China	Zhong 9A/Zhonghui 218	Hybrid Guofeng No. 2 (NR, R)	7.8	11.4
	II-3A/Zhonghui 218	Hybrid II You 218 (NR, R)	8.3	18.6
	Shanyou 46	Yield standard	7.0	-

that produce trehalose at 3-10 times the normal rate, resulting in tolerance to drought and/or salinity have been developed by introducing the *ots A* and *ots B* genes for trehalose biosynthesis from *Escherichia coli* into rice (Garg *et al.* 2002). In China, Chinese researchers have developed several GM rice varieties that are resistant to the country's major rice pests and diseases, such as the stem borer, bacteria blight, rice blast fungus and rice dwarf virus. Significant progress has also been made with drought – and salt-tolerant varieties of GM rice, which have been in field trials since 1998 (Jia *et al.* 2004).

Perhaps one of the most promising, despite controversies, application of transgenic technology in rice has been the development of Vitamin A-enriched rice, popularly known as Golden Rice™ due to the slight yellow color conferred on the rice endosperm in transgenic grains (Potrykus 2000, Beyer *et al.* 2002). Vitamin A is considered as absolutely essential for children and women of child bearing age and, worldwide, nearly 134 million children are at risk for diseases related to Vitamin A deficiency (VAD), including some 3.1 million preschool age children who suffer from eye damage, and nearly 2 million children under 5 years of age that die each year from diseases linked to persistent VAD. In Southeast Asia alone, 5 million children become at least partially blind every year due to VAD. Golden Rice™ has the potential to improve the supply of Vitamin A in the human diet, thereby alleviating the suffering and death of millions of people, especially those who cannot afford diet diversification (ISAAA 2004a). New Vitamin A-enriched materials with up to ten times more the level of pro-Vitamin A are now in the pipeline, including several popular Asian indica varieties such as IR64. Reported to involve "clean" events, without cross-border transfers or antibiotic markers, the new materials are being readied for backcrossing and stability and field testing in 2004, while vitamin A absorption and bioavailability tests are underway or planned in the Philippines, China, and the USA (Datta *et al.* 2003, Coffman *et al.* 2004, Cantrell and Hettel 2004).

Another promising use of transgenic technology to improve human nutrition is in combating iron deficiency, one of the most widespread micronutrient deficiencies worldwide. Deficiency to iron in the human diet affects about 3.5 billion people worldwide and could result in illnesses such as anemia, heart problems, and neurological disorders. The ferritin gene from *Phaseolus vulgaris* has already been introduced into rice, resulting in the doubling to tripling of the iron content in the rice endosperm, even after polishing the grain (Vasconcelos *et al.* 2003). To improve the bioavailability of iron, since it is usually in complex with phytic acid, the genes from *Aspergillus fumigatus* encoding a thermotolerant phytase protein and the endogenous cysteine-rich metallothionein-like protein were also introduced into rice resulting in a 7-fold increase in cysteine level and a 130-fold increase in phytase level in the resulting transgenic plants (ISAAA, 2004b).

Many NARES in rice-growing countries of Asia are actively involved in the use of transgenic technologies, encouraged by government policies supporting biotechnology research, and endowed with universities and agricultural research institutes with biotechnology research capacity. In a recent study done by the International Food Policy Research Institute (Atanassov *et al.* 2004), 209 transformation events were reported to have already been done in 76 scientific institutes in 16 countries. Of these, 109 (52 per cent) were done in 7 Asian countries, viz., China (30), Indonesia (24), India (21), the Philippines (17), Thailand (7), Pakistan (5), and Malaysia (5). Of these countries, however, only the Philippines had so far approved the commercial release of a transgenic food crop – a Bt-enhanced corn. Although the highest number of transformation events for any crop was reported for rice (17.7 per cent), followed by potatoes (11.0 per cent), maize (8.6 per cent), and papayas (6.2 per cent), a GM rice variety has yet to be commercialized in Asia.

In the Philippines, both IRRI and PhilRice have on-going rice biotechnology programmes employing molecular marker and transgenic technologies, as well as other more conventional techniques such as in vitro culture and wide hybridization. With the Philippine government declaring a policy supportive of biotechnology research, the use of biotechnology is embedded as a strategy for achieving the goals set by the irrigated lowland, direct seeded, rice for fragile environments, and hybrid rice multidisciplinary R&D programmes of PhilRice. GM technology, in particular, is being used to improve high-yielding varieties, including NPTs and hybrid rice parental lines (Aldemita *et al.* 2004). The Philippine focus is on the tungro, sheath blight, blast, and bacterial blight diseases, as well as on the insect stemborer, and tolerance to salinity. Genes procured from laboratories around the world and modified for *Agrobacterium tumefaciens*-mediated transformation, are being used to generate transgenic plants. A number of transgenic plants that contain chitinase and glucanase genes have already been produced and tested under controlled screenhouse conditions. Moreover, PhilRice has conducted the first and only contained field trials for any GM rice in the Philippines where the transgenic IR72 plants containing the *Xa*21 gene for bacterial blight resistance showed complete resistance against nine Philippine races of the pathogen. On the other hand, transgenic plants with the *pin*2 gene are being developed to improve stemborer resistance, while a coat protein gene from the rice tungro bacilliform virus is being used in *A. tumefaciens*-mediated transformation. PhilRice is also a member of the Golden Rice™ Network and undertook backcrossing activities on the now discarded original Golden Rice™ materials. To hasten the availability of vitamin-A enriched rice to consumers, PhilRice hopes to continue its active participation in this network that involves other Asian countries such as Indonesia, Vietnam, India, Bangladesh, and China, as well as partners in developed countries such as the US, Germany, UK, and Switzerland. Already, guidelines are on the national testing of GM rice prior to commercialization are being prepared. To hasten public acceptance of biotechnology, in general, and GM rice, in particular, PhilRice, along with other Philippine government agencies, has also been spearheading a massive public education campaign using the tri-media as well as various public fora involving the government, private, NGO, and religious sectors.

Work in progress. Advances being made in the field of functional genomics will provide ample scope to further increase yield, build plant protection, improve nutrition, and enable rice to grow using less water and in adverse environment. The availability of the complete rice genomic sequence offers a lot of opportunities to further understand the natural genetic variation and the effects of alleles, and their interactions, for traits that are important in rice breeding, using specific genetic backgrounds and under specific environments. At IRRI, for example, biotechnologists are systematically assessing the array of phenotypes resulting from the disruption of putative gene sequences in mutants, near-isogenic lines, permanent mapping populations, and elite and conserved germplasm through a functional genomics initiative (Hossain *et al.* 1997, Leung *et al.* 2004). However, these gene discovery and allele mining efforts would require the annotation of the rice genome and the subsequent build up of databases and information resources. The use of information and communication technology and bioinformatics, such as the IRIS (Bruskiewich *et al.* 2003; http://

www.icis.cgiar.org/) and GeneFlow (www.geneflow.com) databases, should make the mounting information more easily accessible to scientists, especially breeders in rice-growing countries.

Other work in progress include studies designed to transfer the C_4 photosynthetic pathway and leaf anatomy genes of maize to C_3 rice in order to improve the rice plant's radiation use efficiency while reducing transpirational water loss and N fertilizer requirement, and studies aiming to more deeply understand the genetic variation for drought tolerance using genomics and bioinformatics tools in order to identify the exact genes involved (Cantrell and Hettel 2004). Another promising area is the genetically engineering of N2 fixation capacity into rice and, in this direction, attempts to engineer the nif-regulon into the chloroplast genome have been made with the idea of not having to make rice totally independent of external nitrogen supply, but to provide additional nitrogen during the grain filling period to rescue the photosynthetic apparatus for a longer period of time (Potrykus 2000). Over the medium- and long-term, the apomixis research that earlier had been started at IRRI, would need to be vigorously pursued using biotechnology in order to capture and made available to resource poor farmers the benefits of heterosis.

With over 27 million tonnes of rice worth US$5560 million lost annually due to pests such as the stem borer, sheath blight, and bacterial blight, GM rice solutions are nearing commercialization to help offset this yield loss. Ready for field evaluation are Bt/hybrid rice in China and India; XA rice in China, Philippines and India; Golden rice in the US, the Philippines and India; and herbicide tolerant rice in Spain, USA, and China. For commercialization by 2005-06 will be Bt rice in China, and Golden Rice and Ferritin or high- iron rice by 2007-08 (Datta 2004).

Issues, Concerns, and Opportunities

Explicit governmental biotechnology agenda. There is a need for many Asian rice-growing countries to develop clear and time-bound national agenda for biotechnology R&D and commercialization. For example, in the Philippines, a technology explicit and market driven national development agenda, which recognizes the role of science and technology in promoting economic development and facilitating trade is desired, along with corresponding increased investments in R&D (Padolina 2004). This could be achieved by developing a collaborative scheme that shall bridge the academe and science and technology community with industry, and having both well tuned to market demands. There is also a need to emphasize the role of the government in formulating technology policies and plans, as well as funding of research and development projects; the role of academe in identifying what problems need solving, and the role of the private sector in investing research that could meet the country's immediate needs.

In the case of India, for the first time, a specific impetus has been given to the advancement of biotechnology. In the country's 2005-05 budget, the Minister for Finance emphasized that science and technology, including biotechnology, "will receive priority and will be provided with additional funds." A specific provision was given for companies doing scientific R&D approved by the Department of Scientific and Industrial Research before April 1, 2004 to be entitled to 100 per cent deduction of profits for 10 years. The Federation of Indian Chambers of Commerce and Industry noted that this will favour small and medium biotechnology companies who can channel savings to augment R&D activities (Crop Biotech Update 2004a).

The Agricultural and Development Economics Division (ESA) of the Economic and Social Department of the United Nations' Food and Agricultural Organization (FAO) showed that most of the research institutions in China, Cambodia, and Indonesia are in the initial states of developing biotechnology research capacity. The proportion of biotechnology expenditures to the total agricultural research expenditures is very small, and mainly from the public sector. The report discusses the importance of secured and sustained public research capacity including physical, human and financial, in the successful development of biotechnology innovations. For instance, countries like China, India, Indonesia, Malaysia, Philippines, Argentina, Brazil and Bulgaria have made significant investments in biotechnology research and regulation. Experience with genetically modified organism (GMO) testing for a wide array of locally important traits, and commercialization in these countries is growing, and government support programmes and policies actively encourage biotechnology R&D.

In China, scientists have released a report urging the central government to allow the commercial planting of genetically modified (GM) rice (Zhu 2004). They note that GM rice technologies are technically mature and are ready to be commercialized. GM products include several rice varieties resistant to China's major rice pests, including those that can resist the stemborer by using *Bacillus thuringiensis* (Bt), delta endotoxin and cowpea trypsin inhibitor CpTI genes, a protease inhibitor rice, a planthopper and bacterial leaf blight resistant rice using the Xa21 gene, and fungus-resistant rice (The Business Daily Update, 2004). The country currently has the largest field for GM rice trials. An estimate of about 25-30 per cent of China's plant biotechnology investments are spent on GM rice programmes (Zhu 2004). China has increased its budget for research and field trials of GM rice since 2001. Its biotech budget for 2001-2005 is $1.2 billion, a 400 per cent increase compared with 1996-2000. About $120 million out of the current budget is devoted to GM rice programmes (Jia *et al.* 2004). The Chinese Government has become the world's second-largest spender on plant biotechnologies, next only to the United States and the country is expected to launch at least 10 GM rice field trials by 2005 and release *Bacillus thuringensis* (Bt), cowpea trypsin inhibitor gene, and *Xa21* gene GM rices that year. Already, field trials in Hunan and Fujian provinces showed that GM rice boosted yields by 4 to 8 per cent, and allowed an 80 per cent reduction in pesticide use (Crop Biotech Update 2004d).

Setting the biotechnology R&D priorities. It may be argued that most of the earlier rice biotechnology activities, particularly in the public sector and on transgenic technology applications, were more science-driven and researcher-driven than attuned to the needs of ordinary farmers. It is important to note that for GM rices to be useful, at least in the immediate term, and to gain fast acceptance amongst resource poor farmers, it is best that they be derived from varieties already widely grown and suited to specific agroenvironments (DFID 2004). Ranged against the challenges confronting rice cultivation in most Asian rice growing countries today, it is clear that international as well as NARES biotechnology research should focus, on one hand, on the most important rice diseases and pests, and physiological and environmental factors that reduce rice productivity and quality as discussed earlier, and on the other hand, on increasing rice yield potential. An example of trait prioritization for rice biotechnology research in Asia, aimed at delivering the greatest impact on the lives of poor rice farmers and consumers, while being complementary to conventional rice improvement efforts, has been put forward by Hossain *et al.* (1997, Table 3). To ensure relevancy of biotechnology R&D agenda, a bottom-up approach needs to be implemented in the crafting of R&D priorities, where farmers' and other stakeholders' needs and concerns are adequately addressed. Such approach should benefit from the rich

Table 3. Prioritization of traits for biotechnology intervention in different rice growing environments (Hossain et al 1997).

Priority traits		Target environment	Available products breeding	Preferred approaches*		
				Conventional selection	Marker-aided	Transgenic
Stresstolerance	Bacterialblight	Rainfedlowland transgenic lines	Genes,markers,	++	++++	++++
	Sheathblight	Irrigated,High yield	Transgeniclines	+	+	++++
	Blast	Upland	Markers	+++	+++	+
	Stemborer	All	Transgeniclines	+	0	++++
	Drought	Rainfedlowland, Upland	Underdevelopment	++	+	+
	Salinity	Coastal areas		+++	+	++
Nutritionalvalue	Vitamin A	transgeniclines	Geneconstructs,	+	0	++++
	Fe		Geneconstructs	+++	0	+++
	Zn			+	0	?
Yield enhancement		All ecosystem	Elite lines	++++	++	++

*More '+' marks indicate higher priority; 0 = not applicable.

indigenous knowledge of local farming communities on specific rice production constraints while facilitating public acceptance and ensuring the trickling down of benefits from biotechnology-derived products. The extent to which biotechnology may improve food security does not settle the question of its relevance to quality of life; it is essential to move stakeholder involvement upstream in setting research priorities and to fairly share benefits through appropriate infrastructure and ownership arrangements (Chadwick 2004).

Need for more public investments. There remains an imbalance on R&D investments on rice biotechnology that tend to favour developed countries, thus impacting on the potential of biotechnology to boost agriculture in the developing world and alleviate the plight of resource-poor rice farmers in Asia. The concentration of biotechnology R&D in developed countries and the limited private sector effort in developing countries, particularly in Asia, has raised concerns over the economic concentration of biotechnology in favour of developed countries and multinational companies (ADB 2001). As the private sector would be unlikely to undertake rice biotechnology research based primarily on the pressing needs of resource poor farmers, due to difficulty in recovering costly investments, there is need for significant public-sector funding initiatives if benefits are to reach resource-poor farmers in developing countries in order for them to develop pro-poor biotechnology R&D agenda. Furthermore, public research products would have to gain similar approval as those developed by the private sector if transgenic research products and their associated potential benefits are to reach the poor. In this context, it will be necessary to work with local communities to ensure acceptance and adoption from the bottom up rather than simply again trying to impose viewpoints from the top down. Thus, needs must be identified – nutritional and environmental– so that product traits are country-relevant (National Agricultural Biotechnology Council 2004).

While Asian scientists have demonstrated the capacity to successfully undertake biotechnology R&D relevant to the needs of resource-poor farmers, the desired phenotypes have been few when compared to traits being developed by multinational firms and advanced research institutes in the developed world (Nuffield Council on Bioethics 2004). One bright spot, however, has been the case of Thailand that established the National Center for Genetic Engineering and Biotechnology (BIOTEC) in 1983. BIOTEC has supported biotechnology

R&D in six areas, including the improvement of disease resistance in rice, particularly rice blast. This disease affected 200,000 hectares of rice in Thailand in 1993, causing serious economic loss and resulting in government intervention to assist disease-struck farmers worth about US$10 million. Since then, BIOTEC has supported research for the molecular genetic characterization of local blast isolates and mapping of resistance blast genes, with focus on aromatic varieties for Thailand's export rice market. In 1999, BIOTEC also provided US$3.7 million to fund the 'Rice Genome Project Thailand', particularly for the sequencing of rice chromosome 9 that contains a QTL for tolerance to a very important concern of Thai rice farmers-submergence (Tanticharoen 1997). Most rice growing countries in Asia, with the exception of China and India (Atanassov *et al.* 2004), however, have yet to launch similarly focused government initiatives on rice biotechnology R&D. In China, investments on public sector biotechnology research has risen dramatically to $1.2 billion for 2001-2005, a 400 per cent increase over 1996-2000 levels, with about $120 million allocated for transgenic rice R&D (Jia *et al.* 2004). With field testing on various transgenic rices already going-on since 1998, with 53 hectares planted in 2003, China is poised to becoming the first country in the world to commercialize transgenic rice.

Importance of collaborations. Given the varying biotechnology research capacities of rice-growing NARES and the limited resources allocated for biotechnology research in the public sector, unintentionally encouraged by the phasing out of the IPRB of the Rockefeller Foundation (O'Toole *et al.* 2001), the constraints in NARES R&D budgetary allocations, and the reduction of funding support for international agricultural research centers (IARCs) such as IRRI (Cantrell and Hettel 2004), the need for biotechnology R&D practitioners to collaborate has become paramount. Collaborations need to be pursued at the individual, institutional, governmental, bilateral, regional, and international levels to ensure not only that the highest returns for R&D investments are attained, but also to facilitate regulatory approvals and biotechnology product commercialization. At the national level, the creation of a national coordinating body such as BIOTEC in Thailand (Tanticharoen 1997) should provide a mechanism for increasing efficiency in the use of limited national R&D budgetary allocations through the avoidance of research duplications and sharing of in-country research capacities. In the Philippines, the recent creation of a Crops Biotechnology Center under the Department of Agriculture augurs well for the development of a unified biotechnology R&D agenda for the country's priority crops, including rice, and the optimization of the use of limited manpower and logistical resources. On the other hand, a regional collaboration approach, as exemplified by the ARBN (Leung *et al.* 2004) should be able to develop a biotechnology R&D agenda focused on the shared needs of rice farmers in the region and, where possible, human pool, scientific, and financial resources or, alternatively, parcel out the research portfolio as was done in the rice genome sequencing initiative. One type of formal collaboration that has yet to be explored involves bilateral arrangements between countries. In the development of transgenic technologies, these South-to-South collaborations would be facilitative to the build-up and sharing of common approaches, genes, germplasm, regulatory trials, and biosafety-related information (Atanassov *et al.* 2004). The already established broad-based regional cooperation, such as the Association of Southeast Asian Nations (ASEAN) and the Asia Pacific Economic Conference (APEC) should be tapped to support these regional biotechnology undertakings. At the international level, programmes that help rice scientists from developing countries to train, further hone their capacities, and maintain ties with advanced laboratories at IARCs and developed countries need to be supported. For instance, India's Department of Biotechnology (DPT) and the United States for International Development have signed a letter of intent to initiate enhanced cooperation in agricultural biotechnology research and development. The partnership will pursue agri-biotech research projects including technology development, technology diffusion, biosafety, and related policy activities. In addition, joint workshops, conferences, scientific exchanges, and training of scientists will also be done. The programme will increase the "range of safe and environmentally sound technological options to producers and consumers of agricultural products" (Crop Biotech Update 2004a).

Role of IARCs and the private sector. Without formal, dynamic, and synergistic interfaces between the public and private sectors, much of the benefits of crop biotechnology will not reach those who need them the most. The sharing of information and experiences across sectors is crucial to facilitate the flow and process that technologies undergo from the laboratory to the farm (Crop Biotech Update 2004b). With many NARES still not fully enabled to undertake, solely by themselves, activities spanning the whole biotechnology research, development, and commercialization spectrum, IRRI and similar international institutions will still need to play their roles as technology and knowledge providers, as well as builders and enhancers of biotechnology capacities of rice-growing NARES. Of particular importance for IRRI is the provision of strategic research outputs that already several NARES in Asian countries are capable of transforming into applications and products. These could include protocols, gene constructs, and markers for traits relevant to local problems but prohibitively expensive for NARES to develop by themselves. Alternatively, IRRI should be able to complement its strategic research programme with a product development thrust, focusing on biotechnology-derived advanced breeding lines and varieties, with traits that have common high relevance amongst Asian countries. The product development portfolio could include varieties tolerant to drought, of high nutritional value, and resistant to major diseases such as tungro and bacterial blight. The role of IRRI as facilitator in the transfer of useful technologies and products amongst NARES through the sharing of technologies, knowledge, and experiences need to be strengthened. Equally important is its role in facilitating the formation of effective NARES/public sector and private sector collaborations, for NARES to be able to access private sector-held intellectual property (IP) on rice biotechnology processes and products. IRRI can also serve as a clearinghouse for IP-protected technologies from both the public and private sectors that NARES can easily access. Training support by IRRI and similar institutions for NARES should now also include those designed to advance NARES capacity on the science and management of biotechnology, IPR, biosafety and food safety regulation, and international negotiations. As Cantrell and Hettel (2004) argued, with IRRI's strengths, it can serve as the unbiased broker and facilitator amongst the rice NARES, advanced research institutions, and the private sector.

Other international organizations, such as the FAO, can help expedite rice biotechnology progress in Asia by promoting and supporting networking mechanisms such as the South-to-South cooperation model. They can also help in developing and supporting infrastructure for public-good agricultural research, providing knowledge and training to NARES researchers, enabling interactions amongst biotechnology stakeholders through dialogues and similar fora, facilitating access to relevant IP, sensitizing policymakers on biotechnology-related issues, and assisting governments in the crafting of biotechnology-related policies. As the primary source of GM crops continues to be the private sector, technology transfer between private and public sectors, in terms of products as well as experiences on regulation, commercial development, and release of GM crops, would greatly benefit NARES. This technology transfer can be facilitated by private foundations such as the International Service for the Acquisition of Agri-Biotech Applications (ISAAA).

Intellectual property rights (IPR). The impact of IPR on biotechnology research is often imbedded in discussions on public and private sector partnerships. There is a need to balance the fact that on one hand public sector institutions, due to limited resources, cannot fully avoid accessing private sector-held IP during the development of its own products and, on the other hand, the private sector has to avail of IPR protection to be able to protect its investments and commercial interests as well to be able to share their IP with other sectors without fear of exploitation. The development of the Golden Rice™ is a case in point. In total, 70 IPRs and technical property rights (TPRs) belonging to 32 different companies and universities were used in product development and for which 'freedom-to-operate' situations had to be applied for in order for NARES to begin using Golden Rice™ in further breeding and in de novo transformation activities using locally adapted varieties (Potrykus 2000). Several modalities, however, are still open to the public sector to be able to access genes and technologies from the private sector. These include direct purchase of genes and technologies, licensing, the fact that patents have time limits, confidential agreements, and the purchase of genes for incorporation into local germplasm. New types of IP agreements have also evolved, such as the donation of IP facilities and 'humanitarian' use type agreements as were done with Golden Rice™ with the threshold for humanitarian versus commercial use being a $10,000 income from the technology. The agribusiness giant Syngenta recently announced that it would donate new Golden Rice seeds and lines to the Golden Rice Humanitarian Board, including scientific results of the first field trials, as well as the technology, rights, and research results (Crop Biotech Update 2004d).

As the issue of IPR is likely to become increasingly important, the capacities of governments or the science sectors of many developing countries to understand, deploy, and negotiate regarding biotechnology need to be strengthened. Rice biotechnology practitioners in Asia need to be trained on the details of modern IPR systems and on negotiating with institutions and companies for the purpose of accessing IP, and applying for IP protection. Alternatively, research institutions could establish IP units, not only for negotiating with other institutions and sectors, but also for the IP registration of their own biotechnology processes and products.

Regulatory requirements. National biosafety committees in developing countries have made impressive progress in the drafting and implementation of biosafety regulations for the importation and testing of transgenic crops, with regulations for field tests already in place in rice-growing countries such as China, India, Thailand, and the Philippines (Atanassov *et al.* 2004). A looming issue, however, revolve around the compliance costs for regulatory approval that could prohibit many developing country institutions. In the various studies cited by Atanassov *et al.* (2004), annual compliance costs, including initial greenhouse and field screening, field testing for environmental impact, and food safety, but excluding technology development costs, ranged from US$140,000 for a virus-resistant papaya in Brazil to US$830,000 for a virus resistant potato in South Africa. For rice, an annual regulatory compliance cost of US$680,000 was estimated for a virus resistant variety in Costa Rica (Sittenfeld 2002) covering tests on molecular characterization and epidemiology, transgenic field trials, biosafety, IPR, food safety deployment, and gene flow. Given reduced NARES budgets, this could pose a major hurdle in the commercialization of rice biotechnology products from the public sector. It is hoped, however, that as knowledge and experience is gained by regulatory agencies, approval costs may decrease, both by reducing the number of required tests, and by shortening the length of experimentation. The latter would also avoid the risk of biotechnology products becoming irrelevant to farmers' needs due to approval delays (Atanassov *et al.* 2004). In this regard, continuous training of personnel from regulatory bodies of developing countries on new biotechnology developments and approaches is necessary for them to make educated recommendations, as is envisioned in the Cartagena Biosafety Protocol (CBD 2000). A well functioning regulatory system can hasten public acceptance of biotechnology products by instilling public confidence that the risk assessments conducted are carefully done, science-based, and, therefore, safe. While international harmonization of standards may be required, there is also need for contract-sensitivity that is appropriate to the place in which a technology will be applied (National Agricultural Biotechnology Council 2004).

Policy support. Policy initiatives are necessary to accelerate investments by technology holders and adoption by the farming communities in Asia. The Indian government, for example, is formulating new policies to boost investments and research in the local biotechnology sector. These include promoting the speedy approval of GM crops, and funding and infrastructure support for public-private partnership programmes plant biotechnology, among other areas (Sinha 2004). The new policies will also provide the framework for research and business institutions, and illustrate the trade and investment guidelines for the newly emerging biotech sector. A group of experts will also be set up to suggest models for public-private partnerships in the biotech sector. The biotechnology department will invest the creation of innovation centers with the existing academic and research institutions (Bhan 2004). To date, Delhi University has been identified to be the first center to receive the funding. Other cities such as Hyderabad, Pune, Chennai, Ahmedabad, and Lucknow will also be the focus of the development. Similarly, in Taiwan, Premier Yu Shyi-kun pledged his commitment to establish a Biotech Industry Strategy Consulting Committee, which would consolidate and integrate the country's biotech-based promotion organizations and research institutes (Crop Biotech Update 2004c).

Aside from policy initiatives, transparent protocols must also be established and international guidelines followed. There is also the need to establish a world-class intellectual property rights regime for biotechnology inventions and the protection of plant varieties. In addition, concurrent and transparent trials for biosafety for both new and released events are necessary and a determined drive against illegal genetically modified seeds trade is important.

Biosafety and food safety. Biotechnology is a very powerful tool that can be used in the developing world to grow more rice in an environmentally friendly manner. It can improve food production by making farming more efficient. The benefits that biotechnology confers upon the environment include the reduction in the use of agrochemicals and the preservation of presently uncultivated and marginal lands and their concomitant biodiversity due to increases in productivity in the more favorable environments. To sustain the rice agriculture resource base and avoid environmental disturbance, it is important to match new genes and biotechnology-derived varieties to the conditions of the target environments (Atanassov *et al.* 2004). As commercialized GM crops by 2003 in the developing world was largely limited to insect-protected cotton in Argentina, China, India, Mexico, and South Africa (James 2003), there is still limited experience on food safety assessments to draw from for a food crop such as rice. Among developing countries, only three have approved a single transgenic event in a food crop (soybean in Brazil, Czech Republic and Uruguay; and maize in the Philippines), two have approved two events (soybean and tomato in Mexico; soybean and maize in South Africa) and one (Korea) has approved three events (one in soybean and two in maize) (Atanassov *et al.* 2004). Therefore, the sharing of experiences and knowledge from the food safety assessments done in these countries should be valuable for developing countries with rice biotechnology products in the pre-commercialization stages. As rice is a food crop, and per capita rice consumption could vary both in-country and among countries, from less than 100 kg/yr in countries like China and India to over a 200 kg/year in countries like Myanmar (Maclean *et al.* 2002), careful food safety experimentation must be done in the case of nutrient-enhanced GM rice to remove potential health dangers related to over dosages, if any, or alternatively, effective GM rice deployment strategies need to be developed.

Communication. Communication plays a vital role in disseminating information. It is a powerful tool in influencing man's decision. Media plays a crucial role in framing public understanding of science. Appreciation of traditional knowledge is essential for science to be communicated successfully. The message will be understood and better appreciated if there is an understanding of local knowledge (Luganda 2004). It is important to understand cultural values, and respect traditional knowledge to successfully communicate science. Scientists, journalists and others involved in the communication of science should take into account cultural factors and local knowledge in their work (Public Communication of Science and Technology, 2004). The adoption and use of biotechnology and genomics should be approached within the context of conventional practices. Rather than view agricultural biotechnology as the wave of the future, we should regard it as part of a mélange of the new and old, balanced appropriately to meet local needs. The point was emphasized that agricultural biotechnology would be more readily adopted, and food security would be more attainable as would environmental sustainability, if it were blended back into conventional practices in order that value-added benefits would accrue alongside maintenance of traditions (NABC 2004).

There are good examples of public education campaigns on biotechnology being done in Asian NARES. In Thailand, the Biotechnology Alliance Association (BAA) has been set up to educate the public about biotechnology applications, including genetically modified crops. Science based information will be provided to the public and several fora will be organized to discuss the benefits and risks of GM crops so that stakeholders can make intelligent decisions relative to biotechnology and its use (Sriwantanapongse 2004). The potential for biotechnology to result in economic, environmental, and social benefits in India is enormous and promotion of the country's first hand experience in this area, through knowledge sharing activities, could serve as a powerful example for other developing countries (ISAAA 2004). In the Philippines, the Biotechnology Association of the Philippines along with the Departments of Agriculture and Science and Technology, have also been mounting information campaigns through public dialogues, media presentations and regular press releases.

Given all these issues and challenges, lessons can be learned from the saga of Golden Rice™, as to the merging of factors necessary for a rice biotechnology product to be developed and commercialized for impact. As detailed by Potrykus (2000), the project was made possible because of the enabling factors such as: (i) environment supportive of independent research; (ii) strong institutional collaborative research partnerships; (iii) availability of the needed genes; (iv) support from donor institutions for strategic research for developing countries; and (v) highly motivated team of scientists willing to work on a pro-poor R&D agenda. He further noted that the Golden Rice™ experience should: (i) facilitate greater public acceptance of GMO technology; (ii) encourage research investments in projects without guarantees for success, (iii) motivate research to be more food security- and less industry-focused; (iv) encourage free licensing for enabling technologies if used for humanitarian purposes; and (v) motivate scientists to undertake projects relevant to the poor.

Conclusion

The application of biotechnology in rice will help many Asian NARES to produce the estimated 700 million tonnes of rice required to feed an additional 650 million rice consumers by 2025. At the same time, it can also help lower the cost of rice farming, and add nutritional value to rice, thus benefiting resource-poor farmers through higher incomes and improved nutrition and health. Moreover, biotechnology may also be harnessed to protect the environment and sustain the natural resource base. The technology, however, must continue to draw its relevance from its being able to address both the existing and projected problems of small rice farming communities and, at the same time, the food and health needs of more than half of the world's population that consumes rice. Furthermore, products must be so designed such that they complement rather than replace existing practices and enrich rather than disrupt the agroenviroments for which they are targeted for deployment. Integration of new science with traditional knowledge would be important in this regard. For the full potential of rice biotechnology to be realized in Asian NARES, the full engagement of and sustained effective communication amongst all stakeholders, at all levels, in the public, private, NGO, and other relevant sectors of society are needed. In these, Asian governments can play a catalytic role by developing responsive programmes and policies to ensure that the benefits of rice biotechnology applications will impact poor farmers and consumers, through a stable household food and economic security, and sustainable rice-based farming systems.

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