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Seeds, Science and US Dominance in the Development and Use of Transgenic Seeds

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Abstract: The United States has moved more quickly to acceptance of the use of genetically modified crop varieties (GMVs) than other countries. The rapid market penetration of GMVs in the US is based on the existence of a large, dynamic seed market, an experienced and predictable regulatory system and a significant public and private sector research capacity. A few large developing countries including Brazil and India are developing their capacity in these areas. A smaller set of institutional capacities are required for a country to access spillover benefits from GMVs developed in other countries.

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Seeds, Science and US Dominance in the Development and Use of Transgenic Seeds

The emergence of practical biotechnology protocols for creating genetically modified plant varieties (GMVs) has transformed the system for supplying improved plant varieties to US farmers. Within three years of the appearance of the first GMVs in the US, more than 500 GMVs were available for field crops. By 2004, transgenics occupied 85% of the total soybean area, 76% of cotton area, and 45% of maize area in the US. Argentina, Canada, China and Brazil also have large areas planted to GMVs, but none of these countries yet has same momentum for the spread of GMVs that the US has.

Three institutional structures are crucial for a country to access GMV technology. First, the scientific capacity in biotechnology and crop improvement must exist. Second, a regulatory system that has the confidence of industry and consumers must be in place. Finally, there must be a dynamic system of seed delivery. In this paper I review the US experience with GMVs and discuss the factors that have contributed to the success of the US biotechnology movement. I examine activity within the scientific, regulatory and commercial seed sectors of US, reviewing data on the origin of transgenic events and their movement into commercial crop varieties.

The scientific and commercial process for generating genetically modified crop varieties

A handful of vertically coordinated firms have been the key players in ushering in the biotechnology revolution in the United States and other countries. These firms have been successful in linking useful genetic events with high quality germplasm to create GMVs with

the ability to gain rapid market penetration and to capture value for the creators. These firms have used mergers, acquisitions and licensing agreements to ally their financial, scientific, and organizational strengths with the genetic resources of traditional seed companies such as Delta and Pineland, Asgrow, Pioneer, Dekalb and dozens of smaller seed companies.

The creation of a commercially viable GMV can be thought of as resulting from combining the products of two largely distinct scientific undertakings - a biotechnology step, and a plant breeding step. The biotechnology step produces a genetic event or gene transformation that is useful in solving an economically important agricultural problem. The gene must then be combined with an adapted crop variety to create a viable commercial GMV. The two steps are largely separate scientific enterprises and need not occur in the same institution, or even in the same country. Most GMVs today are marketed and delivered to farmers by seed companies that do no have the capacity to do genetic transformation. The seed companies license transgenes from Monsanto, or another biotechnology company, and use conventional breeding techniques to transfer the genes into their best commercial lines. Delta and Pineland Seed Company (D&PL), which is one of the world's leading marketer of GMVs, has never had significant biotechnology research capacity. D&PL is a modest size seed company with eight US based cotton breeders and three breeders in other countries[1]. However, the seed companies have extensive experience in marketing seeds to farmers – an important capacity that the multinational gene discoverers do not have.

The type of scientific capacity required to mount a successful biotechnology research program is fundamentally different from that needed for developing adapted crop varieties. Discovering useful genes, transferring them to the intended plant species and achieving an

[1] The totals include breeders working in Paymaster and Suregrow divisions. International breeders are located in Australia, Greece and Turkey.

adequate level of expression of the alien gene in the new plant host is makes use of "new" biotechnology science techniques, while the plant breeding step relies primarily on proven conventional plant breeding techniques. The science of biotechnology itself is evolving rapidly, with a steady stream of process innovations, so this distinction is becoming less valid and the line between the biotechnology and plant breeding is becoming ever more blurred. For example, marker assisted selection is a technique developed by biotechnology research firms, but which is now routinely used by seed companies. The companies that have successfully commercialized transgenes have needed large investments, cutting edge scientific talent, and the skilled legal council needed to negotiate intellectual property (IP) hurdles.

Success in discovering a marketable event is also very uncertain, with many more failures than successes. The end product of the biotechnology step is a crop variety with an adequate level of expression. The transfer of the gene to the initial, or receptor variety is accomplished using one of several biotechnology protocols. Subsequent transfers to other varieties of the same crop are done using traditional plant breeding techniques.

Because the receptor variety is chosen on the basis of its characteristics in expressing the gene, rather than its superior agronomic performance, the plant breeding step is essential to achieve a GMV that will be successful in the market. The plant breeding step for self-pollinating crop varieties is straightforward. The receptor variety is crossed with a leading commercial line, followed by three or four backcross generations and another three selfing generations to attain a genetically stable variety. Using modern breeding practices, it is possible to produce several selection generations per year, so a marketable GMV can be produced from a receptor line in 2-3 years. This plant breeding step of creating a commercial GMV from a receptor GMV is quicker, easier and more certain than the development of a

commercially successful conventional variety from a pool of elite lines, and can be done at a fraction of the cost.

Crop improvement research in the US

The US seed market is supported by a large crop improvement research effort that is shared by three sets of institutions: the Agricultural Research Service/US Department of Agriculture (ARS/USDA), state agricultural experiment stations (SAESs), and private companies. Approximately 1,612 crop improvement scientists were employed in the US in 2001 (Table 1). Biotechnology research has become an important research focus, with 22% of the all US crop improvement researchers conducting biotechnology related research. The private sector employs 63% of all scientists, the SAESs employ 26% and ARS/USDA about 12% (Table 2). This demonstrates the vital role that the private sector has played in the development of US seed and biotechnology research. The difference in intensity of private sector research between the US and other countries is one of the primary reasons that the US has led the way in the use of transgenic technology.

Regulation of GMVs in the US

The regulation of GMVs in the US is a coordinated effort shared by four principal agencies. The USDA's Animal and Plant Health Inspection Service (APHIS) regulates the field testing of GMVs, the Food and Drug Administration (FDA) governs food safety and labeling. The National Institutes of Health has developed guidelines for the laboratory use of genetically engineered organisms. Finally, the Environmental Protection Agency (EPA) ensures the safety and safe use of GMVs in the environment.

Two main steps are involved in clearing a GMV for commercial use. The institution producing a new GMV must first either obtain a permit to conduct field trials or notify APHIS of its intent to conduct field trials of the new "regulated article[2]". Upon completion of several years of field trials, the institution may petition APHIS to have an article removed from regulated status. If the petition is granted, the GMV may be commercialized. Once an article is removed from regulated status, subsequent GMVs of the same crop can be developed without additional approvals if they are produced using conventional plant breeding techniques.

A total of 10,880 total trials were conducted by 242 different institutions in the US between 1987 and May 2005 (Figure 1). An average of 997 trials were conducted annually between 1998 and 2004. The 40 institutions with the most field trials are reported in Table 3. The list includes 12 public and 28 private institutions in top 40. Monsanto has conducted 40% of all trials and nearly a third of the 65 commercial approvals. An average of five commercial approvals per year have been granted since 1992 (Table 4). It is not clear how many different events have been field tested, but a guess would be that less than one in 200 tested events has been approved for commercialization. Twenty-one different private companies have received at least one APHIS commercialization approval. The large life science firms dominate approvals, and approvals are highly concentrated among these institutions. Only Monsanto, AgrEvo, Dow and Calgene have received more that two approvals, and these four companies account for two-thirds all approvals. Just two approvals have been received by public sector institutions (virus resistance in papaya by Cornell, and sulfonylurea tolerant Flax by the University of Saskatchewan), no public sector institution has received a commercialization approval since 1998. The overall regulatory picture in the US, is that the capacity to generate

[2] "Regulated articles are considered to be organisms and products altered or produced through genetic engineering that are plant pests or that there is reason to believe are plant pests." APHIS web page

a GMV and to conduct field trials is widespread, but that the commitment and financial muscle needed to obtain commercial approval is concentrated in large corporations. Large firms possess expertise in negotiating the regulatory process, in dealing with post-approval IPR, and have an ability to handle marketing challenges that public sector and smaller private sector firms do not have.

The US seed market

The US has been the focus of agricultural biotechnology research primarily because of the huge size of its domestic seed market. The US commercial seed market is larger than the combined size of the next two largest markets (Table 5). Because of the value-added that they provide to seeds, the entrance of transgenic products has greatly increased the total value of seed sales in the US. For example, in 2005 Delta & Pineland conventional varieties sell for $26.12 per acres while the most popular transgenic varieties are priced from $43.09 to $61.41 per acre. This provides a powerful incentive for private sector investment in plant breeding research. Worldwide an estimated 70% of biotechnology investments originate in the private sector (Table 6), so this incentive effect is a key factor explaining growth and focus of the industry. The US market accounts for more than 85% of worldwide revenues from licensing of transgenic technologies (Figure 2).

The USDA publishes data on the area covered by each cotton variety. It is useful to examine this data to learn about the effect that transgenics have had on the cotton seed industry. The first commercial cotton GMVs were developed through a strategic alliance between Monsanto and the dominant U.S. seed cotton firm, Delta and Pine Land Company (D&PL). Monsanto chose to introduce Bt cotton through a licensing agreement D&PL.

Initially D&PL was the only seed company to sell transgenic varieties. The elite commercial germplasm for the transgenic varieties was provided by D&PL from two recurrent parent varieties that were popular commercial varieties in the US. The first US Bt varieties, NuCOTN 33^{B} and NuCOTN 35^{B}, were subsequently marketed in several countries without in-country adaptation. In 1996, the first year of commercial availability, Bt cotton was planted on 729,000 ha or 14% of the cotton area in the United States.

The introduction of transgenics in 1996 led to a slight increase in the already-dominant cotton seed market position (based on area) of D&PL (Figure 3). D&PL's market position has fallen to about 50% as other seed companies have added transgenics to their product lines. The number of tansgenic varieties has increased steadily over time (Figure 4) until in 2004 the number of transgenic varieties available exceeded the number of conventional varieties.

By 2004, US farmers could choose from more than 84 different transgenic cotton varieties marketed by nine different companies (Table 7). Six types of cotton GMVs are available in the US: Bt insect resistant varieties, RoundupReady herbicide tolerant varieties, Bt/RR stacked varieties with insect resistance and herbicide tolerance genes, BXN varieties that are tolerant to bromozynil herbicide, Bollgard II varieties with two Bt genes, and Bollgard II/RR varieties with stacked insect resistance and herbicide tolerance. Bt/RR stacked varieties and RR varieties were planted to the largest area in 2004, but there were more RR varieties available than any other type. The average area per GMV is not large at just 53,000 ha. and has been relatively steady through time. This suggests that the marginal cost of developing a new variety is not high, and has important implications for the spread of GM technology to smaller countries.

A Model of the Transfer of GMVs to Developing Countries

How might other, smaller countries, gain access to GMVs? The US, with nearly 100 million ha in major row crops represents a market worthy of large investments, even under uncertain conditions. Under what conditions might other countries exploit spillover opportunities in biotechnology? A cost function model of the variety production process can be used to analyze a firm's decision to attempt to enter a developing country market with a variety. The firm will not enter a market that doesn't satisfy the ex-ante condition that the expected market price for the new variety exceeds the expected average production cost. Figure 5 uses average cost curves to represent the market entry decision for three types of GMVs: 1) a conventional variety being developed from available genetic resources, 2) a GMV being developed by backcrossing a gene from an unadapted US variety to a locally available conventional variety, using a national licensing partner, and 3) directly marketing a US GMV, such as occurred with the first cotton Bt variety, DP 33B. Developing a competitive conventional variety would be the most expensive undertaking; importing a US GMV would be the least expensive. Launching a conventional breeding program implies substantial fixed costs associated with establishing a research facility, assembling a germplasm collection and hiring personnel. Depending on the quality of the initial breeding germplasm, it could take a minimum of 5-10 years to get a product to market, and success is quite uncertain when challenging for a share of the conventional seed market. This explains why private investment in plant breeding research is so small in developing countries.

The limited experience to date with the launch of GMVs in new markets has been one of relatively rapid capture of market share. GMV development costs are quite low compared to the conventional variety case, because the GMV is developed by backcrossing a single gene

into a successful existing variety whose agronomic properties have already gained market acceptance. Fixed costs are very low for the biotechnology firm, since we are assuming that the firm is partnered with a national seed company.

In the case where an existing US-developed GMV is directly introduced into a new market, virtually no fixed costs are incurred since no breeding is done. It requires only that seed be tested, reproduced and marketed. Monsanto has used this type of commission agreement with seed distributors in South Africa, Argentina, Mexico, Australia and other countries.

Within this simple framework, it is clear that the minimum market size needed for a country to entice entry by a multinational biotechnology firm is smaller for GMVs than it is for conventional varieties. Not only are R&D costs lower, but GMVs generally sell at a premium of $15 to $35 per ha. Bt cotton seed sells double the price of conventional varieties in the US. Through the use of a licensing agreement, this premium will be shared between the biotechnology firm and the licensee seed company.

In figure 5, the minimum size for entry would be Q_{min} for a conventional variety, Q_{min}^{*} an adapted GMV and Q_{min}^{**} for an imported GMV. This implies, for example, that Pioneer or Asgrow might choose to enter into GMV partnerships to license their genes to seed companies in countries where they have not tried to breed their own conventional varieties. Because of the price premium on GMV seed, it is also possible that multinationals might choose to enter markets in countries even if it means in investing in setting up a conventional breeding program. Development costs are no higher for a GMV than a conventional variety once the genetic event has occurred.

The above discussion applies to developing country access to GMVs containing genes that are already in use in the US. These events may or may not be useful in addressing problems that are important in tropical countries. The R&D investment required to develop a useful article is far higher than the investment required to adapt an existing article to local germplasm. Multinational companies will invest in biotechnology research for some important developing country problems, but only if those countries represent an attractive potential market. The attractiveness of developing countries in general, for the introduction of GMVs depends on the applicability of the technology as well as the marginal costs of entering new markets. The successful transgenic technologies to date have been highly transferable, more similar to pesticides than to new plant varieties. The fact that research investments may potentially be amortized over markets in several countries provides an incentive for firms to undertake large research investments.

Even if a country does not have the scientific, regulatory and commercial institutional capacity to develop it's own GMVs, it can gain access to spillovers from GMVs developed for other markets. This requires a much less daunting set of institutional capacities. The most important conditions might include the following: 1) the country must have a tested, transparent, science based regulatory process for GMVs, 2) there must be a reasonable ability to protect intellectual property embodied in seed, 3) GMVs should be accepted by farmers, regulators, processors and legislators and, 4) seed markets must be capable of delivering seed to farmers.

Summary

The United States has moved more quickly to acceptance of the use of genetically modified crop varieties (GMVs) than other countries. The rapid market penetration of GMVs in the US is based on the existence of a large, dynamic seed market, an experienced and predictable regulatory system and a significant public and private sector research capacity. A few large developing countries including Brazil and India are developing their capacity in these areas. A smaller set of institutional capacities are required for a country to access spillover benefits from GMVs developed in other countries.

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James, C. "Global Status of Commercialized Biotech/GM Crops: 2004" ISAAA Briefs No. 32-2004. The International Service for the Acquisition of Agri-biotech Applications (ISAAA), Manila, Philippines.

USDA/AMS "Cotton Varieties Planted" Agricultural Marketing Service/USDA, Washington DC, various years

Tables and figures

Figure 1. Number of field tests in US by year 1987- May 2005.

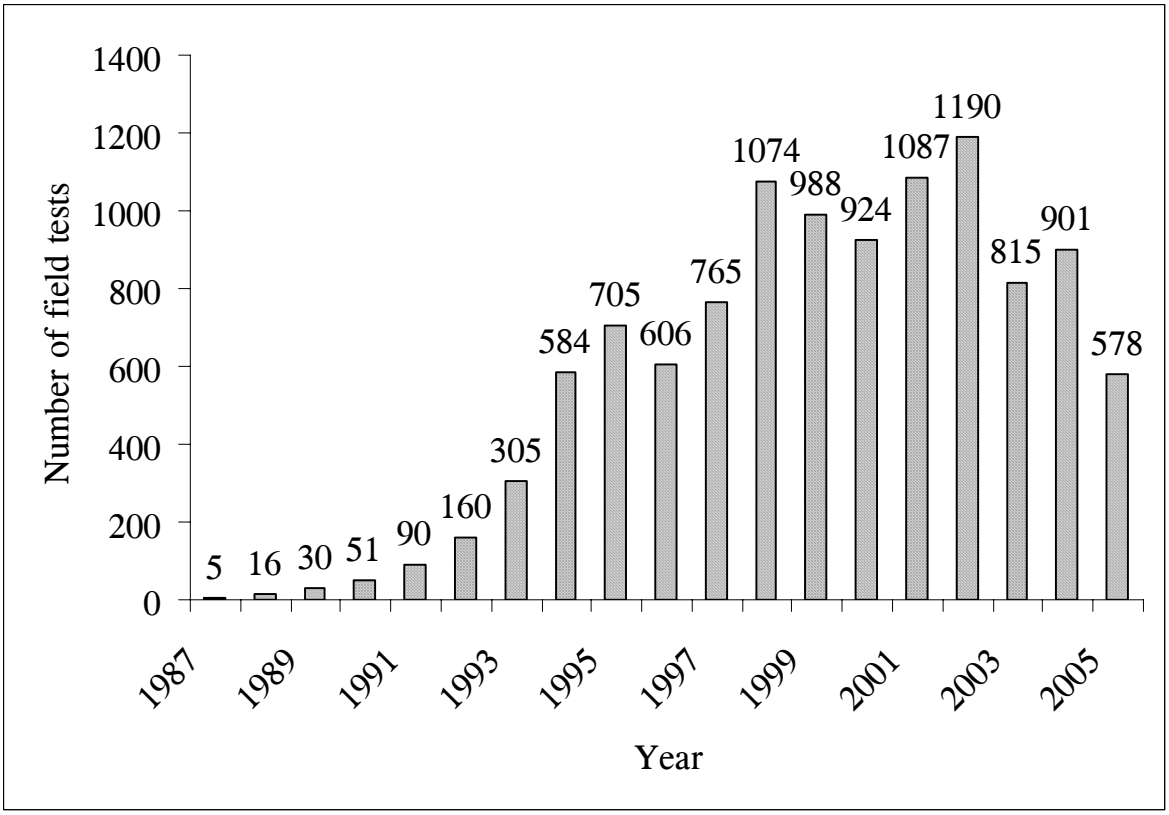
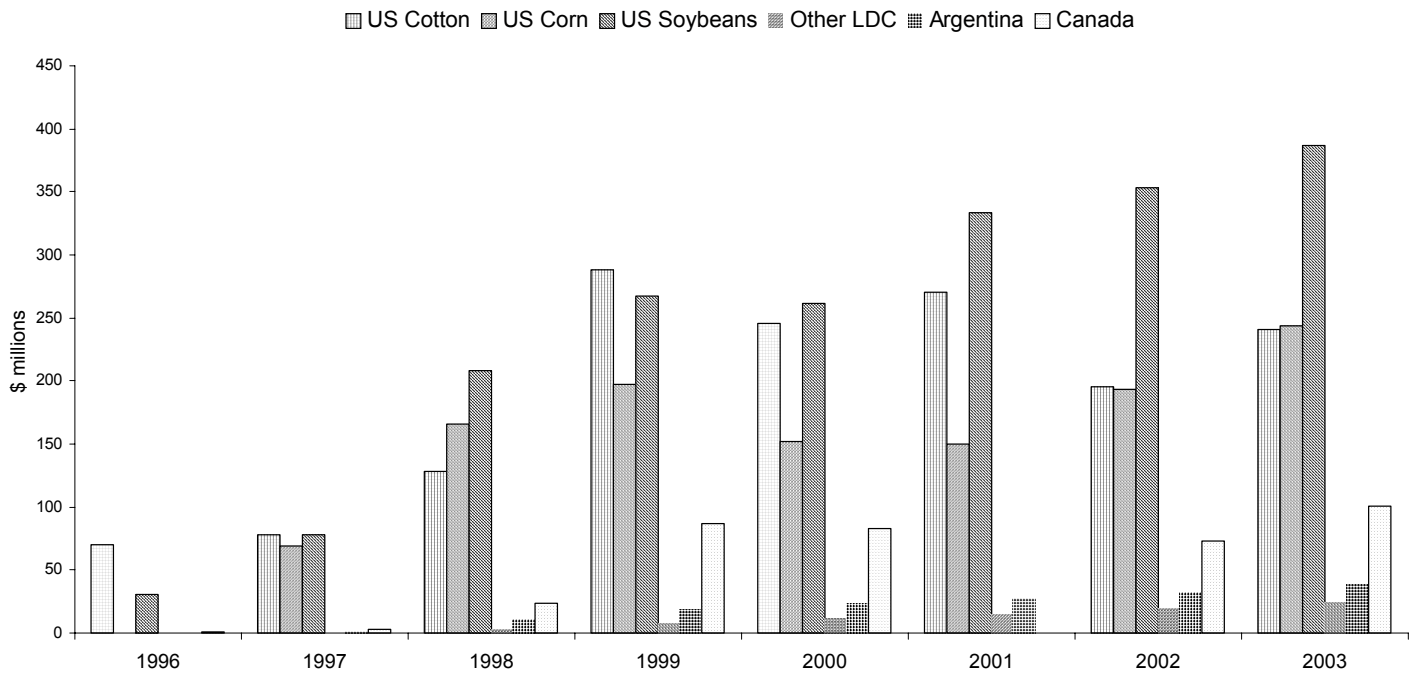
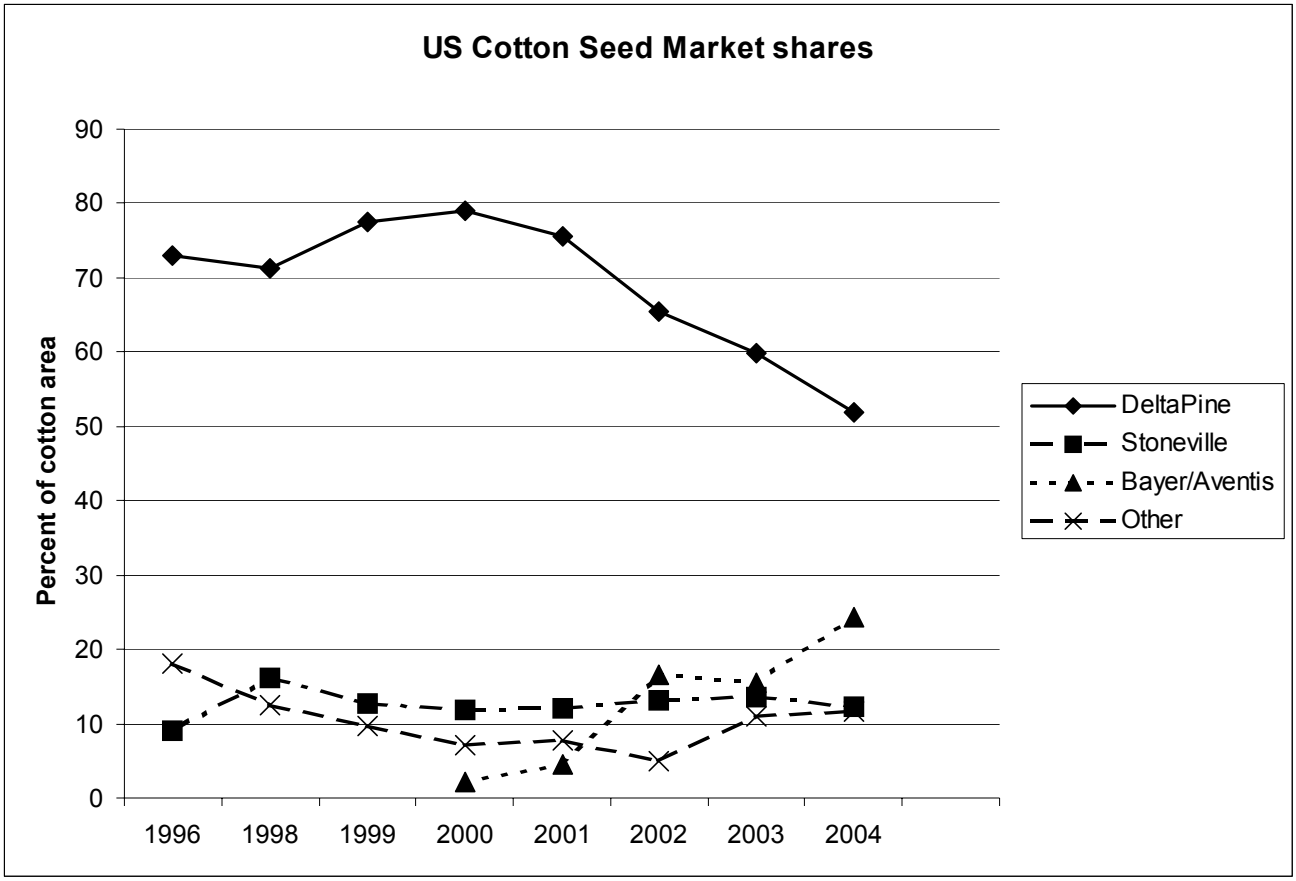


Figure 2. Estimated royalty revenue from GMVs



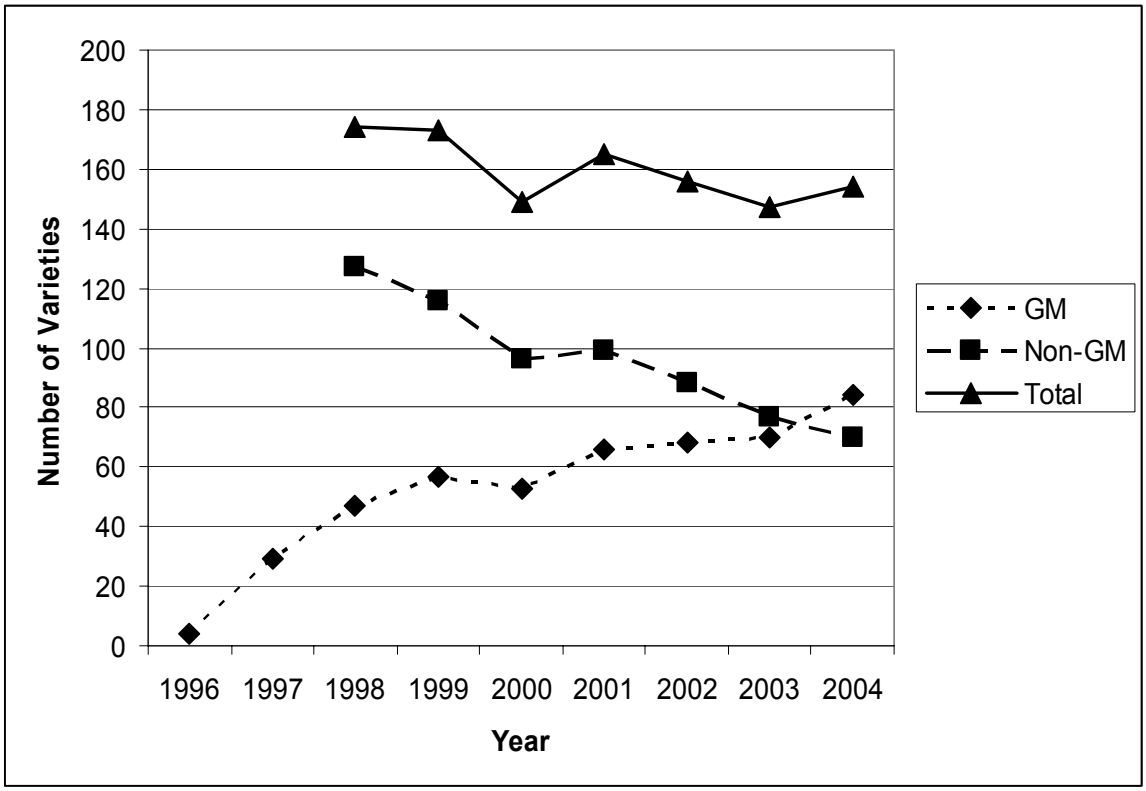
Source: Author's calculations.

Figure 3. US cotton area shares by seed company.



Source: USDA/AMS "Cotton Varieties Planted"

Figure 4. Number of cotton varieties available in the US, 1996-2004 (Number of non-GM not available for 1996,1997)



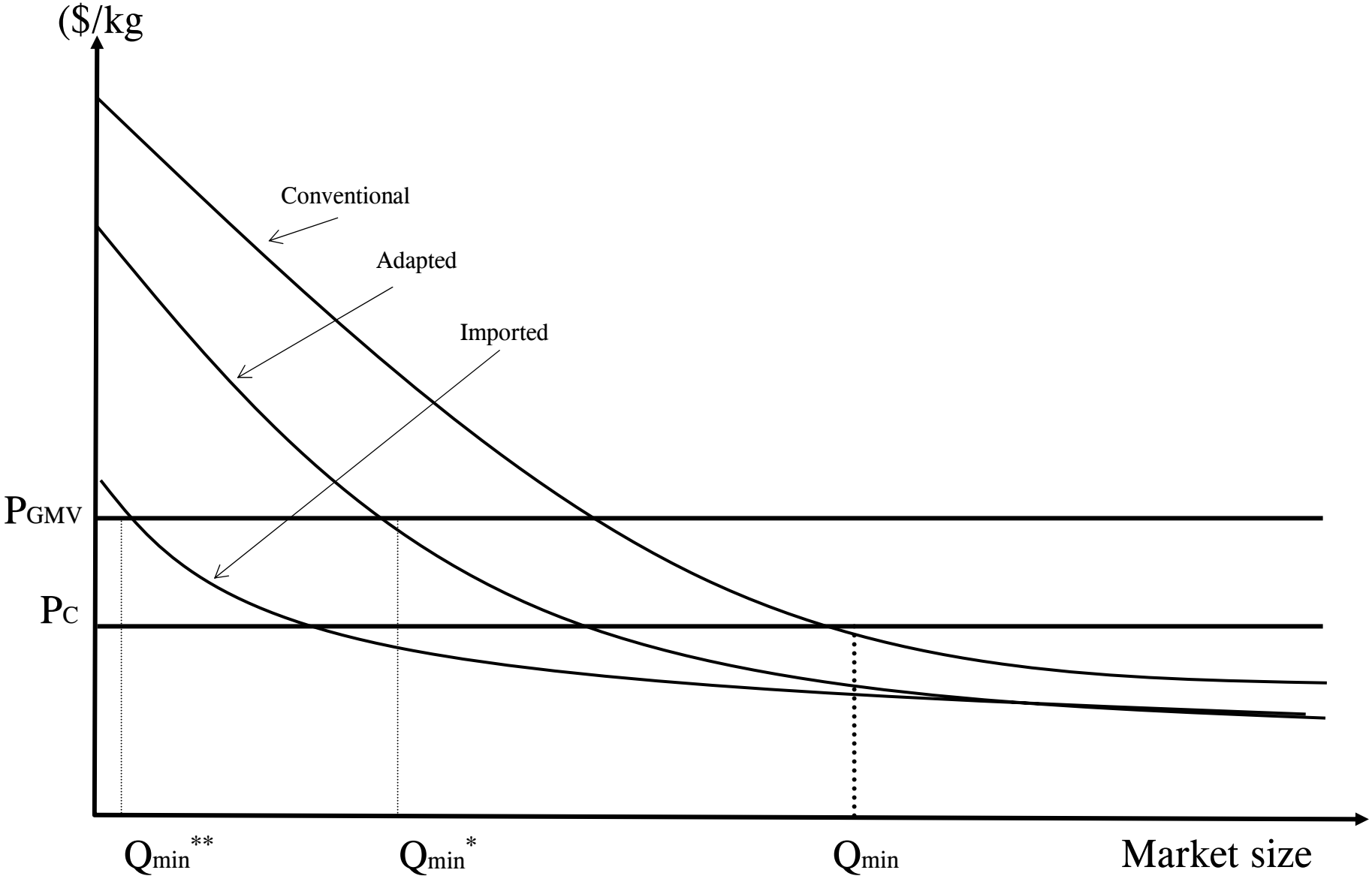


Figure 5. Average cost curves and minimum market size required for market entry for conventional varieties, adapted GMVs, and imported GMVs

Table 1. Numbers and percentages of plant breeding SYs devoted to plant breeding research, germplasm enhancement, cultivar development, and biotechnology R&D arranged by employer.

Category	SAES		ARS/USDA		Private industry		Activity totals	
	Num.	Pct.	Num.	Pct.	Num.	Pct.	Num.	Pct.
Plant breeding research	83	20%	108	58%	161	16%	352	22%
Germplasm enhancement	70	17%			82	8%	152	9%
Cultivar development	143	34%			612	61%	756	47%
Biotechnology R&D	121	29%	80	42%	152	15%	353	22%
Totals	416	100%	188	100%	1,008	100%	1,612	100%

Source: Author's survey (Preliminary results, do not cite)

Table 2. Private sector breeders as a percentage of total plant breeders by research area,

	SAES	ARS	Private	Total
Plant breeding research	32%	5%	63%	100%
Germplasm enhancement	34%	26%	40%	100%
Cultivar development	18%	5%	77%	100%
Biotechnology R&D	34%	23%	43%	100%
All Research	26%	12%	63%	100%

Source: Author's survey (Preliminary results, do not cite

Table 3. Numbers of field trials and commercial approval of the 40 institutions with the most field trials, 1987- May 2005.

Rank	Institution	Number of trials	Cumulative number of trials	Cumulative Percent of trials	Number of approvals
1	Monsanto	4,396	4,396	40%	21
2	Pioneer	633	5,029	46%	1
3	AgrEvo	326	5,355	49%	9
4	Du Pont	320	5,675	52%	2
5	ARS	249	5,924	54%	
6	Seminis	199	6,123	56%	
7	Syngenta	182	6,305	58%	
8	DeKalb	181	6,486	60%	2
9	Calgene	164	6,650	61%	9
10	Scotts	150	6,800	63%	
11	Dow	132	6,932	64%	4
12	Aventis	122	7,054	65%	1
13	Iowa State U	115	7,169	66%	
14	ArborGen	104	7,273	67%	
15	Rutgers U	97	7,370	68%	
16	U of Idaho	96	7,466	69%	
17	Betaseed	94	7,560	69%	
18	ProdiGene	90	7,650	70%	
19	DNA Plant Tech	89	7,739	71%	1
20	Stine Biotechnology	86	7,825	72%	
21	U of Florida	83	7,908	73%	
22	Northrup King	80	7,988	73%	1
23	Novartis Seeds	77	8,065	74%	2
24	U of Kentucky	75	8,140	75%	
25	Asgrow	75	8,215	76%	1
26	Upjohn	73	8,288	76%	1
27	U of Nebraska	69	8,357	77%	
28	Cargill	65	8,422	77%	
29	Oregon State U	65	8,487	78%	
30	Agracetus	61	8,548	79%	
31	Harris Moran	61	8,609	79%	
32	U of Arizona	56	8,665	80%	
33	Stanford U	54	8,719	80%	
34	Frito Lay	54	8,773	81%	
35	Agritope	53	8,826	81%	1
36	Michigan State U	51	8,877	82%	
37	North Carolina State	50	8,927	82%	
38	Zeneca	50	8,977	83%	1
39	PetoSeed	50	9,027	83%	
40	Bayer CropScience	46	9,073	83%	

Source: Information Systems for Biotechnology, http://www.isb.vt.edu/2002menu/regulatory_information.cfm

Table 4. Number of commercial approvals in the US, 1992-2004

Year	Number of Approvals
1992	1
1993	0
1994	6
1995	12
1996	10
1997	6
1998	9
1999	6
2000	2
2001	1
2002	5
2003	2
2004	5
Total	65

Source: Information Systems for Biotechnology website, http://www.isb.vt.edu/2002menu/regulatory_information.cfm

TABLE 5 - Estimated size of the domestic market for seed and other planting material of selected countries, 2005 (in USD million)

Country	Size of domestic market	Country	Size of domestic market
USA	5,700	Egypt	140
China	3,000	Belgium	130
Japan	2,500	Chile	120
France	1,930	Serbia & Montenegro	120
Brazil	1,500	Nigeria	120
Germany	1,000	Finland	103
India	1000	New Zealand	90
Argentina	930	Slovakia	90
Italy	780	Switzerland	80
Canada	550	Paraguay	70
Russian Federation	500	Tunisia	70
Korea	400	Uruguay	70
Australia	400	Bangladesh	60
Mexico	350	Portugal	60
Taiwan	300	Ireland	60
Spain	300	Israel	50
Poland	260	Kenya	50
Czech Republic	200	Colombia	40
United Kingdom	257	Bolivia	35
Turkey	250	Zimbabwe	30
Netherlands	208	Peru	30
South Africa	217	Slovenia	30
Hungary	200	Saudi Arabia	18
Denmark	170	Zambia	15
Austria	170	Ecuador	12
Morocco	160	Malawi	10
Sweden	155	Dominican Republic	7
Greece	140	Uganda	6
		Total = 25,243 *	

* This total represents the sum of the commercial seed markets of the listed countries. The commercial world seed market is assessed at approximately US$ 30 billion.

Source: INTERNATIONAL SEED FEDERATION accessed at http://www.worldseed.org/statistics.htm on 5/21/05.

Table 6. Estimated Global R&D Expenditures on Crop Biotechnology, 2001

	$ millions	
Private (70%)	3,100	
Public (30%)	1,120	
Industrial Country Tot. (96%)		**4,220**
China	115	
India	25	
Brazil	15	
Others	25	
Developing Country Tot. (4%)		**180**
World Total		**4,400**

Source: James, 2002

Table 7. Number of cotton varieties, total area and average area per variety by trait, US 1996-2004

Year	B2	Bt	Bt + RR	B2 + RR	BXN	RR	All GM	Tot. Conv.	Total
Number of varieties available									
1996		2	0		2	0	4	na	na
1997		12	3		2	12	29	na	na
1998		17	12		3	15	47	127	174
1999		19	17		3	18	57	116	173
2000		13	20		3	17	53	96	149
2001		10	24		4	28	66	99	165
2002		11	22		5	30	68	88	156
2003	1	9	22	2	4	32	70	77	147
2004	1	7	25	7	3	41	84	70	154
Total Area (1,000 ha)									
1996		697	0		8	0	705	5,123	5,828
1997		986	24		63	184	1,257	4,269	5,526
1998		1,042	192		315	926	2,475	2,906	5,381
1999		1,626	0		na	2,288	3,914	2,304	6,218
2000		944	1,259		na	1,637	3,840	1,900	5,740
2001		212	1,985		213	1,667	4,077	1,230	5,307
2002		637	1,078		142	1,764	3,620	1,279	4,899
2003	0	754	1,454	10	25	1,724	3,967	1,420	5,386
2004	0	918	1,722	81	13	1,722	4,456	1,283	5,739
Avg. Area/variety (1,000 ha)									
1996		349	--		4		177	na	na
1997		82	5		32	15	43	na	na
1998		58	14		91	64	51	22	
1999		49	52		na	67	61	21	
2000		49	82		na	101	83	15	
2001		21	83		53	60	62	12	
2002		58	49		28	59	53	15	
2003		84	66	5	6	54	57	18	
2004		131	69	12	4	42	53	18	

Source: USDA/AMS "Cotton Varieties Planted"

B2=Bollgard II, Bt=*Bacillus thuringiensis kurstaki* insect resistance, RR= Roundup Ready, Bt+RR=Stacked, BXN=bromoxynil tolerant

na=information not available