# Regulatory slowdown on GM crop decisions

#### To the editor:

The speed of regulatory decision-making is an important constraint on the ability of industry to innovate and bring new products to market. To determine whether the US federal government's regulation of biotech crops has become more or less efficient and effective over time, I have analyzed eleven years of information from the US Food and Drug Administration (FDA) and the Animal and Plant Health Inspection Service (APHIS) of the US Department of Agriculture about genetically modified (GM) crops that have passed the mandatory or voluntary regulatory hurdles required before a crop can be commercialized in the United States. The analysis shows that the time it took each agency to reach a regulatory decision more than doubled in the past five years for no explainable reason (see Table 1). That trend should worry those who believe that genetic engineering can be used safely and can benefit farmers, consumers and the environment in the United States, other developed countries and developing countries. Public discourse is needed to understand what factors account for the trends and whether and how they can be

Three federal agencies—APHIS, FDA and the US Environmental Protection Agency (EPA)—regulate GM crops using existing statutes that govern health, safety and environmental impacts of similar products produced by traditional methods<sup>1</sup>. I do not consider the EPA registration process here because that regulatory process only covers a small percentage of GM crops, whereas all GM crops go through APHIS and FDA.

From information publicly available from FDA and APHIS, one can calculate the period of time from the official submission of a regulatory package by a developer to the final agency decision allowing that product to be commercialized. For submissions to FDA under its voluntary consultation process, FDA provides on its website the date when a particular submission is

received by the agency and the date when it sends a letter to the developer stating that the consultation is completed. For the APHIS petition for nonregulated status, its website (http://www.aphis.usda.gov/brs/ informational resources.html) provides both the date when a petition has been received by the agency as well as the date when the petition for nonregulated status was approved. Thus, one can calculate the length of time that each agency took to decide on a particular submission to determine whether the length of time has increased, decreased or remained the same. For both agencies, the number of months was counted from the submission date to the agency decision document, rounding off the time periods to the nearest month.

For the 67 voluntary consultation reviews conducted by FDA between 1994 and 2005, the time from official submission to receipt of the FDA letter ranged from one month (in 1995) to 35 months (in 1995), with an average of 8.5 months per consultation (see **Supplementary Table 1** online). For submissions from 1995 through 2000, the average completion time was 6.5 months. However, for submissions from 2001 to 2005, the average completion time was 15.2 months. Thus, it took FDA 2.3 times as long to review GM crops for food safety from 2001 to 2005 than it did from 1995 to 2000.

For the 70 petitions for nonregulated status ruled upon by APHIS between 1994 and 2005, the decision time ranged from one month (in 1995 and 1996) to 29 months (in 1994), with an average of 8.6 months (see **Supplementary Table 2** online). For submissions from 1994 through 2000, the average completion time was 6.1 months; for submissions from 2001 to 2005, however, the average completion time was 15.4 months. Thus, the review time at APHIS increased 2.5-fold for the period from 2001 to 2005.

The publicly available information from FDA and USDA also allows one to compare the review time for similar products with similar risk profiles. For example, in

September 1994, St. Louis-based Monsanto submitted to FDA its consultation data package for its soybean containing the enolpyruvylshikimate-3-phosphate synthase (EPSPS) gene for tolerance to the herbicide glyphosate and received the conclusion letter from FDA five months later (Biotechnology Notification File (BNF) no. 1). Monsanto also submitted consultation packages in the 1990s for placing that same EPSPS gene into cotton, corn and sugar beets, with the review time for those applications taking five months (BNF no. 26), six months (BNF no. 51) and five months (BNF no. 56), respectively. Thus, the average time for FDA to review crops transformed only with the EPSPS gene in the 1990s was 5.25 months.

Monsanto also submitted voluntary consultation packages for engineering creeping bentgrass, wheat, alfalfa, sugar beet and cotton with the EPSPS gene from 2001 to 2005. In those cases, the FDA review time was 12 months for creeping bentgrass (BNF no. 79), 25 months for wheat (BNF no. 80), 14 months for alfalfa (BNF no. 84), 16 months for sugar beet (BNF no. 90) and 9 months for cotton (BNF no. 98), for an average of 15.2 months. Although the crops are different and each product has a unique transformation event, one would expect the food safety risk analysis of those crops to overlap tremendously, making subsequent reviews quicker. Each crop has the same introduced gene producing the same gene product and two of the major potential food-safety risks one assesses for engineered crops—allergenicity and toxicity—are specific to the gene and gene product, and unrelated to the specific crop. Thus, it seems unlikely that the food-safety risk profile of the particular engineered crops between 2001 and 2005 could explain the almost three times longer review process.

A similar analysis was performed on the publicly available APHIS information to see if engineered crops with similar risk profiles had similar agency review times before and after 2001. For the potential agricultural and environmental risks that are the primary risk issues addressed in USDA's petition for nonregulated status regulatory process, the crop and its phenotype play a determinative role in the engineered crop's risk profile. Thus, if one looks at corn engineered with a phenotype that is both lepidopteran resistant and herbicide tolerant, two such applications were submitted to APHIS in the 1990s, one by Berlin-based AgrEvo (now part of Aventis

Table 1	Average	number	of mon	ths for	US	government	review	and	decision	on
GM crop	S									

Time period	Average number of months USDA took to approve GM crop petitions for nonregulated status	Average number of months FDA took to complete voluntary consultations for GM crops
1994–2005	8.6	8.55
1994–2000	6.1	6.5
2001–2005	15.4	15.2

CropScience) that was decided by APHIS in eight months (97-265-01) and one by Monsanto that was decided in six months (96-317-01), for an average review time of seven months. Two applications for corn engineered with that phenotype were also submitted after 2001, one by Mycogen (San Diego), Dow AgroSciences (Indianapolis, IN, USA) and Pioneer Hi-Bred (Des Moines, IA, USA) that was decided by APHIS in 13 months (00-136-01) and one by Dow that was decided by APHIS in 16 months (03-181-01), for an average time of 14.5 months. Thus, as with the FDA's review process for Monsanto's herbicide-tolerant products, APHIS took significantly longer reviewing corn products with similar risk profiles after

Data from submissions to APHIS involving cotton engineered with a phenotype to be herbicide tolerant also supports the conclusion that the increased length of the review time is not due solely to the potential risks of the product. Three petitions for nonregulated status for herbicide-tolerant cotton were submitted in the 1990s and the APHIS's granting of those petitions took seven months (Calgene (Davis, CA, USA; now part of Monsanto) no. 93-196-01), five months (Monsanto no. 95-045-01) and four months (DuPont (Wilmington, DE, USA) 95-256-01), for an average review time of 5.3 months. For the two petitions for similar products after 2000, the APHIS review time was 13 months (Aventis no. 02-042-01) and 9 months (Monsanto no. 04-086-01) for an average review time of 11 months.

Thus, although the US government tells the American public and the rest of the world that its biosafety regulatory system is fair, efficient and science based, in reality that system has become surprisingly slow at making decisions. One would expect that the regulatory pathway for biotech crops in the 21st century would be quicker and easier than in the 1990s for four reasons: first, regulators have become more experienced with products of this new technology; second, there has been no evidence of risks from any of the existing products; third, with fewer products to review between 2001 and 2005 (75% of all GM crops submitted to FDA and APHIS were concluded by 2000)<sup>2,3</sup>, there should be more agency resources for each product; and fourth, many of the recent products have similar risk profiles to products reviewed in the 1990s. Even so, the time needed to make a regulatory decision has more than doubled at both APHIS and FDA in the past five years. In fact, this slower approach at APHIS has occurred

during a time when APHIS consolidated its resources to regulate GM crops more efficiently and effectively<sup>4</sup>.

APHIS announced almost two years ago that it might be revising its regulatory system for GM crops, but APHIS has not released the proposal to the public<sup>5</sup>. Revising APHIS's regulatory process to make its case-by-case assessment of individual crops a more risk-based system with different regulatory pathways for different potential products would be a start toward making the US biosafety regulatory system more efficient and effective. Both FDA and APHIS need to ensure that all future products receive an efficient review that is proportionate to the potential risks posed by a particular application. GM crops that are not novel and have been engineered with genes already used in previous applications should receive streamlined reviews commensurate with their lower risk so that scarce agency resources could be targeted to novel applications.

On the basis of the analysis in this paper, the US government needs to explain to the public why its 'science-based' regulatory system is taking longer to come to decisions about the safety of GM crops. The public wants assurances that federal regulators are ensuring the safety of products and are not considering nonscientific issues in regulatory decisions, which potentially could result in consumers losing confidence in the

regulatory process. Similarly, unnecessary regulatory delay hurts developers by increasing uncertainty about the regulatory decision-making process and by increasing the cost of getting a product to market.

It has been 11 years since the first commercialized GM crops, and yet only a small fraction of the potential benefits from this powerful technology have been realized. The trends outlined here need to be analyzed and addressed if future benefits are to be realized. Only with a regulatory system that is efficient, transparent and protective of human health and the environment will the US public garner the benefits (and be protected from the risks) of GM crops.

Note: Supplementary information is available on the Nature Biotechnology website.

#### Gregory Jaffe

Biotechnology Project, Center for Science in the Public Interest, 1875 Connecticut Ave., NW #300, Washington, DC 20009, USA. e-mail: gjaffe@cspinet.org

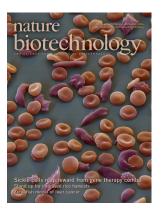
- Office of Science and Technology Policy (OSTP) Coordinated framework for regulation of biotechnology products. Fed Register 51, 23302 (1986).
- 2. http://www.isb.vt.edu/cfdocs/biopetitions1.cfm
- 3. http://www.cfsan.fda.gov/~Ird/biocon.html
- United States Department of Agriculture (USDA). Statement: USDA Creates New Biotechnology Unit (http://www.aphis.usda.gov/lpa/news/2002/08/bio-reorg.html) August 2, 2002.
- United States Department of Agriculture (USDA). Animal and Plant Health Inspection Service (APHIS). Fed Register 69, 3271–3272 (2004).

# Ecological risk assessment for **Bt** crops

#### To the editor:

In their Perspective on commercialized *Bacillus* thuringiensis (*Bt*) toxin transgenic crops and biological control in the January issue (*Nat. Biotechnol.* **24**, 63–71, 2006), Jörg Romeis *et al.* draws some conclusions that do not fully and accurately represent the published data, and more importantly make several

recommendations for ecological risk assessment (ERA) that are unduly narrow and restrictive. In this letter, we focus on the role of laboratory studies in ERA and



discuss the significance of the limitations in their perspective.

One of their main conclusions is that "there is no indication of direct effects of *Bt* plants on natural enemies, either in direct plant feeding assays or when natural enemies have been provided with unsusceptible hosts/ prey containing the Cry toxin." This conclusion is

premature and will require substantially more data. First, although there are many studies on Cry1Ab maize, Cry1Ac cotton and Cry3Aa potato (61 studies), there are only 16

## **Supplementary Table 1**

## FDA Completed Voluntary Consultations for Biotech Crops (1995-2005)10

Year	BNF#10/Food	Submitted to FDA	FDA Letter of Approval	Time Elapsed
1995	#1/ Soybean	September 2, 1994	January 27, 1995	5 months
	#2/ Tomato	August 26, 1994	April 5, 1995	8 months
	#3/ Tomato	September 6, 1994	April 5, 1995	7 months
	#4/ Cotton	June 14, 1994	April 5, 1995	10 months
	#5/ Potato	August 25, 1994	April 5, 1995	8 months
	#6/ Squash	September 6, 1994	April 5, 1995	7 months
	#7/ Tomato	Sept. 16, 1994	April 5, 1995	7 months
	#13/ Cotton	Nov. 21, 1994	June 1, 1995	7 months
	#20/ Oilseed Rape	April 3, 1995	Sept. 26, 1995	5 months
	#23/ Oilseed Rape	March 17, 1995	April 20, 1995	1 month
	#24/ Corn	March 2, 1995	July 14, 1995	4 months
	#25/ Oilseed Rape	August 17, 1992	July 13, 1995	35 months
	#26/ Cotton	April 13, 1995	September 8, 1995	5 months
	#29/ Corn	August 29, 1995	Dec. 14, 1995	4 months
1996	#14/ Tomato	January 16, 1996	March 20, 1996	2 months
	#17/ Corn	October 25, 1995	May 22, 1996	7 months
	#18/ Corn	Sept. 15, 1995	July 24, 1996	10 months
	#28/ Corn	Nov. 17, 1995	March 8, 1996	4 months
	#30/ Cotton	February 21, 1996	June 28, 1996	4 months
	#31/ Corn	January 12, 1996	June 7, 1996	5 months
	#32/ Oilseed Rape	July 6, 1995	April 4, 1996	9 months
	#32/ Oilseed Rape	July 6, 1995	April 4, 1996	9 months
	#33/ Potato	January 24, 1996	April 4, 1996	3 months
	#34/ Corn	June 6, 1996	Sept. 25, 1996	3 months
	#35/ Corn	July 2, 1996	November 5, 1996	4 months
1997	#39/ Soybean	August 28, 1996	March 14, 1997	7 months
	#40/ Corn	Sept. 30, 1996	March 11, 1997	6 months
	#42/ Papaya	January 3, 1997	Sept. 19, 1997	8 months
	#43/ Squash	February 26, 1997	July 10, 1997	5 months
	#45/ Radicchio	May 20, 1997	October 22, 1997	5 months
	#46/ Canola	May 29, 1997	August 25, 1997	3 months
1998	#36/ Corn	April 15, 1998	Dec. 24, 1998	8 months
	#38/ Sugar beet	June 19, 1998	October 8, 1998	4 months
	#41/ Corn	March 3, 1998	May 29, 1998	3 months
	#47/ Cotton	Sept. 18, 1997	January 28, 1998	4 months
	#48/ Potato	July 21, 1997	January 8, 1998	6 months
	#49/ Potato	August 4, 1997	January 8, 1998	5 months
	#50/ Flax	October 27, 1997	May 15, 1998	7 months
	#51/ Corn	August 20, 1997	February 13, 1998	6 months
	#54/ Tomato	Dec. 22, 1997	February 24, 1998	2 months
	#55/ Soybean	March 31, 1998	May 15, 1998	2 months
	#56/ Sugar beet	June 5, 1998	November 3, 1998	5 months
	#57/ Canola	May 29, 1998	Sept. 16, 1998	4 months
		May 29, 1998	Sept. 16, 1998	4 months
	#57/ Canola	Wiay /4 Tyyx	Teni in 1998	1 4 moning

	D. W. 11 (0.1 (0.1 )	7. 7. 1000	D 1 0 1000	
	BNF #60/ Cantaloupe	May 5, 1999	December 9, 1999	7 months
	BNF #64/Canola	May 10, 1999	October 20, 1999	5 months
2000	BNF #63/Rice	Nov. 30, 1999	August 31, 2000	9 months
	BNF #66/Corn	June 7, 1999	April 4, 2000	10 months
	BNF #71/Corn	February 28, 2000	October 18, 2000	8 months
2001	BNF #73/Corn	June 28, 2000	May 18, 2001	11 months
	BNF #75/Corn	Sept. 25, 2000	Dec. 31, 2001	15 months
2002	BNF #74/Cotton	June 29, 2000	July 18, 2002	25 months
	BNF #77/Oilseed Rape	April 30, 2001	Sept. 5, 2002	17 months
	(Canola)			
2003	BNF #79/ Creeping	Sept. 13, 2002	Sept. 23, 2003	12 months
	Bentgrass			
	BNF #86/ Cotton	August 30, 2002	April 2, 2003	8 months
2004	BNF #80/Wheat	June 28, 2002	July 22, 2004	25 months
	BNF #81/Corn	Dec. 11, 2003	October 4, 2004	10 months
	BNF#84/Alfalfa	October 6, 2003	December 10, 2004	14 months
	BNF #85/Cotton	March 17, 2003	May 10, 2004	14 months
	BNF #90/Sugar Beet	April 16, 2003	August 17, 2004	16 months
	BNF #92/Cotton	March 18, 2003	August 3, 2004	17 months
	BNF #93/Corn	June 30, 2003	June 30, 2004	12 months
2005	BFN#87/Corn	August 10, 2004	October 5, 2005	13 months
	BFN#94/Cotton	October 27, 2003	July 8, 2005	20 months
	BFN#97/Corn	March 30, 2004	January 12, 2005	9 months
	BNF#98/Cotton	May 27, 2004	March 7, 2005	9 months

## **Supplementary Table 2**

## Genetically Engineered Crop Petitions Approved by USDA for Non Regulated Status (1994-2005)10

Year	APHIS #/Food	Submitted	Approved	Time Elapsed
1994	92-204-01/Squash	July 13, 1992	December 7, 1994	29 months
	93-196-01/Cotton	July 15, 1993	February 15, 1994	7 months
	93-258-01/Soybean	Sept. 15, 1993	May 19, 1994	8 months
	94-090-01/Rapeseed	March 31, 1994	October 31, 1994	7 months
	94-227-01/Tomato	August 15, 1994	October 3, 1994	2 months
	94-230-01/Tomato	August 18, 1994	Nov. 18, 1994	3 months
1995	94-228-01/Tomato	August 16, 1994	January 17, 1995	5 months
	94-257-01/Potato	Sept. 14, 1994	March 2, 1995	6 months
	94-290-01/Tomato	October 17, 1994	June 6, 1995	8 months
	94-308-01/Cotton	November 4, 1994	June 22, 1995	7 months
	94-319-01/Corn	Nov. 15, 1994	May 17, 1995	6 months
	94-357-01/Corn	Dec. 23, 1994	June 22, 1995	6 months
	95-030-01/Tomato	January 30, 1995	March 23, 1995	2 months
	95-045-01/Cotton	February 14, 1995	July 11, 1995	5 months
	95-053-01/Tomato	Feb. 22, 1995	Sept. 27, 1995	7 months
	95-093-01/Corn	April 3, 1995	August 22, 1995	4 months
	95-145-01/Corn	May 25, 1995	Dec. 19, 1995	7 months
	95-179-01/Tomato	June 28, 1995	July 28, 1995	1 month
1996	95-195-01/Corn	July 14, 1995	January 18, 1996	6 months
	95-228-01/Corn	August 16, 1995	February 22, 1996	6 months
	95-256-01/Cotton	Sept. 13, 1995	January 25, 1996	4 months
	95-324-01/Tomato	Nov. 20, 1995	March 27, 1996	4 months
	95-338-01/Potato	December 4, 1995	May 3, 1996	5 months
	95-352-01/Squash	Dec. 18, 1995	June 14, 1996	6 months
	96-017-01/Corn	January 17, 1996	March 15, 1996	2 months
	96-051-01/Papaya	February 20, 1996	September 5, 1996	7 months
	96-068-01/Soybean	March 8, 1996	July 31, 1996	4 months
	96-248-01/Tomato	September 3, 1996	October 9, 1996	1 month
1997	96-291-01/Corn	October 17, 1996	March 28, 1997	5 months
	96-317-01/Corn	Nov. 12, 1996	May 27, 1997	6 months
	97-008-01/Soybean	January 8, 1997	May 7, 1997	4 months
	97-013-01/Cotton	January 13, 1997	April 30, 1997	3 months
	97-099-01/Corn	April 9, 1997	Nov. 18, 1997	7 months
	97-148-01/Cichorium	May 28, 1997	November 7, 1997	6 months
	Intybus		,	
1998	97-204-01/Potato	July 23, 1997	December 3, 1998	17 months
	97-205-01/Rapeseed	July 24, 1997	January 29, 1998	6 months
	97-265-01/Corn	Sept. 22, 1997	May 8, 1998	8 months
	97-287-01/Tomato	October 14, 1997	March 26, 1998	5 months
	97-336-01/Beet	December 2, 1997	April 28, 1998	4 months
	97-342-01/Corn	December 8, 1997	May 14, 1998	5 months
	98-014-01/Soybean	January 14, 1998	April 30, 1998	3 months
	98-173-01/Beet	June 22, 1998	Dec. 23, 1998	6 months
	98-238-01/Soybean	August 26, 1998	October 14, 1998	2 months

			_	_
1999	98-278-01/Rapeseed	October 5, 1998	March 22, 1999	5 months
	98-329-01/Rice	Nov. 25, 1998	April 15, 1999	5 months
	97-339-01/Potato	December 5, 1997	January 25, 1999	13 months
	98-216-01/Rapeseed	August 4, 1998	January 27, 1999	5 months
	98-335-01/Flax	December 1, 1998	May 19, 1999	5 months
	98-349-01/Corn	Dec. 15, 1998	April 22, 1999	4 months
2000	99-173-01/Potato	June 22, 1999	July 17, 2000	13 months
	00-011-01/Corn	January 11, 2000	Sept. 29, 2000	8 months
2001	00-136-01/Corn	May 15, 2000	June 14, 2001	13 months
2002	01-206-01/Rapeseed	July 25, 2001	Dec. 23, 2002	17 months
	00-342-01/Cotton	December 7, 2000	November 5, 2002	23 months
	01-121-01/Tobacco	May 1, 2001	Sept. 16, 2002	16 months
	01-137-01/Corn	May 17, 2001	October 8, 2002	17 months
	01-206-02/Rapeseed	July 25, 2001	Dec. 23, 2002	17 months
2003	03-036-02/Cotton	February 5, 2003	July 15, 2003	5 months
	01-324-01/Rapeseed	Nov. 20, 2001	January 2, 2003	14 months
	02-042-01/Cotton	February 11, 2002	March 10, 2003	13 months
	03-036-01/Cotton	February 5, 2003	July 15, 2003	5 months
2004	03-036-01/Cotton	February 5, 2003	July 15, 2004	17 months
	03-036-02/Cotton	February 5, 2003	July 15, 2004	17 months
	03-181-01/Corn	June 30, 2003	October 21, 2004	16 months
	04-086-01/Cotton	March 23, 2004	December 20, 2004	9 months
2005	03-155-01/Cotton	June 4, 2003	July 6, 2005	25 months
	03-323-01/Beet	November 19, 2003	March 4, 2005	15 months
	03-353-01/Corn	December 19, 2003	September 23, 2005	21 months
	04-110-01/Alfalfa	April 19, 2004	June 14, 2005	14 months
	04-125-01/Corn	May 4, 2004	December 14, 2005	19 months