The global pipeline of GM crops out to 2020

Claudia Parisi, Pascal Tillie & Emilio Rodríguez-Cerezo

Although a few arable crops and agronomic traits will likely dominate commercial varieties for the foreseeable future, with many being stacked together, more quality traits and specialty crops are being introduced into the pipeline.

The number of countries cultivating genetically modified (GM) crops increased in 2014, with transgenic hectarage reaching 181.5 million[1]. A growing number of companies and research institutes worldwide use genetic engineering to breed new crop varieties, not only for food and feed uses, but also for industrial purposes. Previous studies have documented an increase in innovation in the R&D pipeline for GM crops[2,3], but even an active R&D pipeline would not guarantee commercialization. As with any other technology, economic, market and regulatory considerations act as barriers and reduce the number of R&D products that eventually become commercial. Building long-term projections for commercial GM crops and traits based on the screening of scientific literature is therefore fraught with uncertainty. However, medium-term projections are feasible by screening regulatory pipelines. Given that crop genetic engineering is regulated worldwide, interest in projections for policy makers is high, particularly in terms of raising awareness of potential trade-related issues associated with asynchrony in GM crop authorization globally.

In 2008, the European Commission's Joint Research Centre (JRC) analyzed the global pipeline of GM crops due to reach market in 2015 (ref. 4). That pipeline was dominated by GM soybeans, cotton, maize and oilseed rape, modified mainly for herbicide tolerance and insect resistance, and produced mainly by multinational companies from industrialized countries. The authors foresaw for the following years a scenario in which crop composition traits would slowly emerge, and a larger variety of crops would be developed and marketed, a sizable share of which would be generated by developing countries, especially from Asia and Latin America.

European Commission, Joint Research Centre, Institute for Prospective Technological Studies, Seville, Spain.
e-mail: *Claudia.parisi@ec.europa.eu*

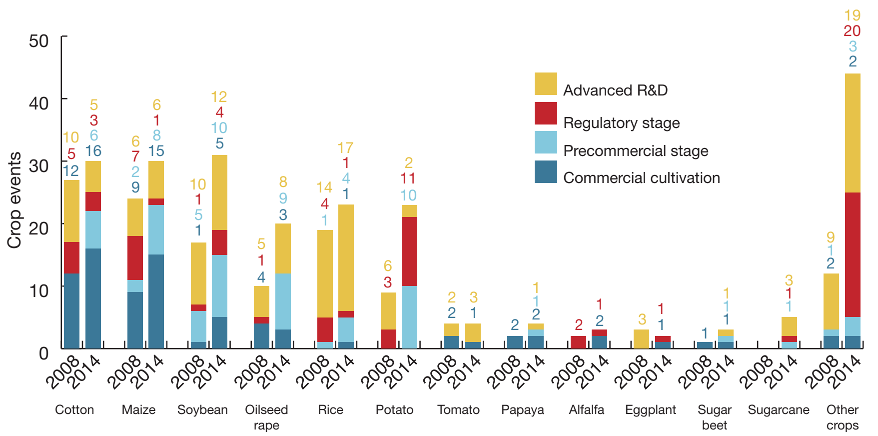

Figure 1 GM crop events in the market and at the precommercial, regulatory and advanced R&D stages in 2008 and 2014, illustrated by crop. Commercial cultivation corresponds to commercialized GM events (those currently marketed in at least one country); precommercial stage refers to GM events authorized in at least one country, but not yet commercialized (commercialization depends only on the decision by the developer); regulatory stage corresponds to GM events already in the regulatory process to be marketed in at least one country; and advanced R&D stage corresponds to GM events not yet in the regulatory process but at late stages of development (large-scale, multilocation field trials, generation of data for the authorization dossier).

Here we update this previous JRC study by depicting the global situation of GM crops in development, including events available on the market and those at the precommercial, regulatory and R&D stages. Our main objectives are to portray the medium-term innovations for the food, feed and industrial sectors, to describe the technical evolution of a growing global pipeline of new GM crops and to analyze the probability of future incidents of low-level presence of unapproved GM material in crop shipments. Our study also analyzes the role of developing countries in the current GM crop pipeline. Finally, we discuss recent developments in plant biotech that may influence the marketing of agbiotech products, in particular the current expiry of important GM crop patents and emerging new plant breeding techniques.

Global evolution of the GM crop pipeline

In addition to GM crop events already in commercial cultivation, the pipeline of GM crops from 2008 to 2014 that we describe here comprises GM crop transformation events (i.e., plants resulting from a unique DNA recombination event) that satisfy one of the following features: first, they have already been approved for cultivation in at least one country (precommercial stage); second, they are under assessment for approval in at least one country (regulatory stage); or third, they are already at late stages of development (advanced R&D stage).

As a first step, we compiled a database from different sources: public databases of approved GM crops, databases of the public authorities responsible for GMO risk assessment, and information available online on the GM crop pipelines of private companies. To validate and complement this information, we organized

Table 1 Overview of the global pipeline of GM crops 2014[a]

Crop	Stage					Type of traits			Number of countries where GM crops are cultivated			Number of countries where GM crops are authorized for import		
	Commercial	Precommercial	Regulatory	Advanced development	Total events	Agronomic	Agronomic + quality	Quality	1 to 2	3 to 5	>5	≤ 8	9 to 16	>16
Cotton	16	6	3	5	30	29	0	0	4	3	4	7	3	3
Maize	15	8	1	6	30	28	0	2	7	2	5	1	9	7
Soybeans	5	10	4	12	31	27	2	2	3	1	1	0	4	5
OSR	3	9	0	8	20	16	0	4	2	1	0	3	3	0
Fruits (tree)	2	2	2	4	10	7	0	3	2	0	0	2	0	0
Vegetable	3	0	2	6	11	9	0	2	2	0	0	2	0	0
Alfalfa	2	0	1	0	3	2	0	1	2	0	0	2	0	0
Rice	1	4	1	17	23	18	0	5	1	0	0	1	0	0
Industrial crops	1	1	13	5	20	16	0	4	1	0	0	1	0	0
Sugar beet	1	1	0	1	3	3	0	0	1	0	0	0	1	0
Potato	0	10	11	2	23	12	0	11	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Sugarcane	0	1	1	3	5	5	0	3	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Leguminous crops	0	1	0	4	5	3	0	0	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Cereals (others)	0	0	3	3	6	5	0	1	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Fruits (ground)	0	0	1	1	2	3	1	0	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Total	49	53	43	77	222	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

[a]The distribution of GM crop events is shown according to development stage, traits and national authorization. The total number of countries where GM crops are cultivated may be an underestimation due to missing data about commercial cultivation of certain GM crops (as explained in the **Supplementary Note**).

an international workshop in June 2014 with a panel of national regulators, public and private GM crop technology providers, international organizations and relevant stakeholders. For a more detailed description of the methodology followed in the data collection, including the limitations encountered, see **Supplementary Note**.

Table 1 summarizes the distribution of GM events in the four development stages, per crop and trait category. In 2014, 49 GM events were in commercial cultivation and 53 events were at the precommercial stage, making a total of 102 GM events authorized in at least one country. We identified 43 events at the regulatory stage and at least 77 GM events at the advanced R&D stage.

In **Table 2**, we looked at the evolution of the GM crop pipeline by comparing our 2008 analysis[5] with data for 2014. Most GM events that were in commercial cultivation in 2008 (90.9%) remained in this category in 2014, whereas 9.1% had been removed from the market. This corresponds to three GM events: a virus-resistant squash developed in the United States, a GM tomato with a long shelf-life developed in China and an herbicide-tolerant oilseed rape, which may all have encountered unfavorable market conditions[2].

During the 2008–2014 period, GM events at the precommercial stage moved up to commercial cultivation (44.4%), remained at the precommercial stage (33.3%) or were removed from the pipeline (22.2%). Of the events we identified at the regulatory stage in 2008, 30.4% reached commercial cultivation and 21.7% reached the precommercial stage in 2014.

The analysis of 2014 data revealed a large number of events that were not identified in the 2008 study in any of the pipeline categories. Some have appeared in the commercial cultivation category, including five events of maize, soybean and cotton marketed by the main GM private developers and two events of cotton and poplar developed in China. Also many events undetected in 2008 (38) have appeared in the 2014 pipeline at the precommercial stage, mostly common arable crops developed by well-known multinational companies. Public institutes and small-to-medium–sized enterprises (SMEs)—especially US- and India-based developers—are responsible for the remaining new GM crops identified between 2008 and 2014 at precommercial stage and are dominant at the regulatory stage (30 out of 38).

Assuming that the same dynamic observed over the 2008–2014 period will be maintained between 2014 and 2020, we estimate the number of GM crop events expected in the market and in the other development stages by 2020 (**Table 2**). According to our projections, a total of 219 GM crop events might be authorized by 2020 (of which 96 events would be in commercial cultivation and the rest at the precommercial stage).

Finally, 20% of GM events identified in advanced R&D stage had progressed to commercial cultivation, precommercial stage or the regulatory stage by 2014. We have not been able to identify the current status of more than half of the 2008 advanced R&D events. We assume that several R&D projects were discontinued, as frequently happens, and therefore did not move through the next development stages. Other possible limitations of our approach are explained in the **Supplementary Note**.

Several reasons may in fact explain why some GM events have not reached commercialization since 2008: unfavorable market

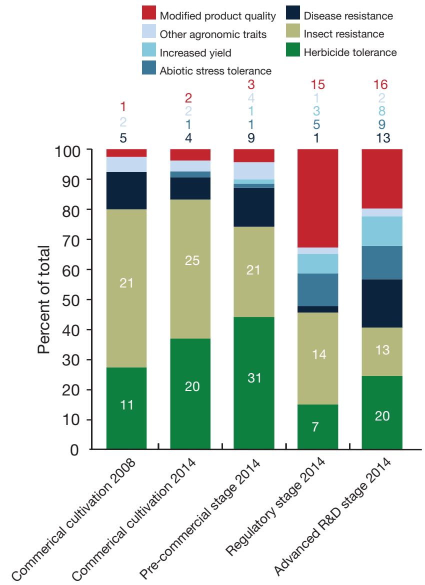

Figure 2 Distribution of traits among GM crop transformation events in commercial cultivation in 2008 and in 2014, and at the precommercial and regulatory stages in 2014. For a more detailed description of the traits present in different stages of the GM pipeline, see **Supplementary Table 1**.

conditions, GM events at the advanced R&D stage not performing as expected when moving to large-scale cultivation, negative public perception that discouraged developers from continuing toward commercialization or the challenge of unaffordable regulatory costs[6]. Based on the data collected, we observe that the share of GM events developed by SMEs and public institutions is higher in the lowest development stages, before reaching the market (data not shown). In fact, they might encounter more budgetary constraints related to regulatory requirements than large companies.

Table 2 Evolution of global GM crop pipeline[a]

2008		2014					
		Status of 2008 products					2020 projected totals
Stage	Number of products	Stage	Number	Percentage	New crops in 2014	2014 totals	
Commercial cultivation	33	Commercial cultivation	30	90.9	7	49	96
		Removed from the market	3	9.1			
Precommercial stage	9	Commercial cultivation	4	44.4	38	53	123
		Precommercial stage	3	33.3			
		Removed from the pipeline	2	22.2			
Regulatory stage	23	Commercial cultivation	7	30.4	38	43	At least 52
		Precommercial stage	5	21.7			
		Regulatory stage	0	0.0			
		Removed from the pipeline	2	8.7			
		No available information	9	39.1			
Advanced R&D stage	65	Commercial cultivation	1	1.5	64	77	At least 89
		Precommercial stage	7	10.8			
		Regulatory stage	5	7.7			
		Advanced R&D stage	13	20.0			
		Removed from the pipeline	3	4.6			
		No available information	36	55.4			

[a]Pipeline shown from 2008 to 2014, with consequent projections for 2020. Projections have been made assuming that 'No available information' on crops means they are no longer in the pipeline (or count as new crops but with different characteristics).

Crops and traits

The landscape of GM crop events in commercial cultivation or at the precommercial stage continues to be dominated by four arable crops: maize, cotton, soybeans and oilseed rape, similarly to the 2008 pipeline (**Fig. 1**); fast followers include GM rice and potatoes, which are poised to reach the market soon and boast a dynamic pipeline of new events. A group of 'other crops' shows substantial growth and are reaching commercial cultivation and the precommercial stage (**Fig. 1**). They include commercial herbicide-tolerant alfalfa, insect-resistant eggplant (Bt Brinjal) and a Chinese insect-resistant poplar. A Brazilian virus-resistant bean, Indonesian drought-tolerant sugarcane and Canadian herbicide-tolerant flax are also at the precommercial stage.

Improved agronomic traits still predominate in commercially cultivated GM crops (**Fig. 2**). Herbicide tolerance and insect resistance are still the prevailing input traits, whereas other agronomic traits are emerging, like virus resistance, abiotic stress tolerance (e.g., drought tolerance) and increased yield. The first commercially available GM drought-tolerant crops (maize and sugarcane) are, respectively, at commercial and precommercial stage in 2014.

Among the herbicide-tolerant events, the pipeline shows new traits that confer tolerance to herbicides beyond glyphosate and glufosinate. Crops tolerant to sulfonylurea, 2,4-D (2,4-dichlorophenoxyacetic acid), dicamba (3,6-dichloro-2-methoxybenzoic acid)[7], isoxaflutole and oxynil are at the precommercial stage in at least one country. Insect-resistant GM events in the pipeline are still directed at *Coleoptera* and *Lepidoptera*, but alternative approaches are being developed through the employment of new *Bacillus thuringiensis* genes.

Quality traits generally refer to modified crop composition and include 'biofortified' crops with a modified nutritional content for food and feed uses and crops with improved industrial characteristics[8]. Their commercial presence is still minor but is increasing in the GM pipeline (**Fig. 2**) and is particularly relevant in current research projects, at an earlier stage of development (not shown in the figure).

The increased number of nutritional traits in the GM crops pipeline is explained not only by technological progress, but also by the market potential and, by a more favorable consumer's opinion[9]. These traits include, among others, modified oil composition for increased content of omega-3 fatty acids or fundamental micronutrients, such as vitamins and amino acids.

GM quality traits for industrial purposes are driven by the search for better sources of biomass for liquid fuels and industrial products. For instance, several countries are commercializing a new variety of GM maize suited for bioethanol production[10]. Soybean and oilseed rape varieties have been genetically modified to adapt their oil profile to the industrial production of biodiesel or other oleo-chemicals[11]. More projects are emerging in the literature, although they are still at a preliminary phase.

Developers of GM crops

As was the case in 2008, most developers of commercial GM crops are multinational companies, with headquarters in the United States or Europe. However, other private companies and public institutions are gaining ground, especially with regards to products advancing to later regulatory stages (**Fig. 3**). The data indicate an increased interest in GM technology, despite the economic costs associated with regulatory approvals in most countries[6].

Most new companies emerging in the GM field are based in the United States and in Asia, especially India, whereas public developers of the technology are appearing in India and China, including at the precommercial stage. Crop developers from South America and Africa are also becoming active in GM crop development (**Fig. 4**). South America is represented in particular by Embrapa, the Brazilian public institute of technological innovation, with two GM events at the precommercial stage.

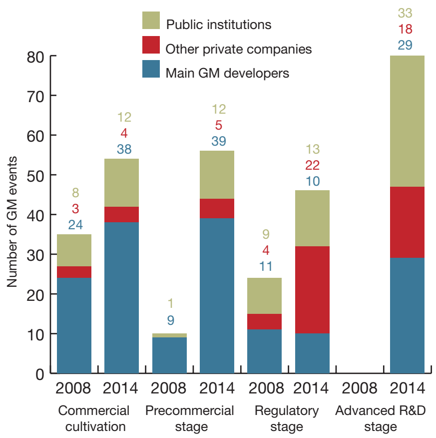

Figure 3 Distribution of GM crop events per developer type and development phase. 'Main GM developers' include BASF, Bayer CropScience, Cargill, Dow AgroSciences, DuPont Pioneer, Monsanto and Syngenta. Data for the advanced R&D stage in 2008 were not included in the former review of the pipeline[5].

In Africa, ten countries are currently developing GM crops, although only four have approved commercial cultivation so far. Companies or institutions from industrialized countries are contributing to the development of GM crops for Africa with adapted agronomic characteristics, including, for example, insect and disease resistance and abiotic stress tolerance[12]. Many of these initiatives are at the advanced R&D phase, some of which also focus on food biofortification to tackle malnutrition issues[12]. They are usually cooperation projects between research institutions from Africa and other countries, such as the projects on GM banana, cowpea and rice coordinated by the African Agricultural Technology Foundation (AATF; Nairobi, Kenya).

GM crop developers from developing countries, such as Brazil, China and India, dedicate more effort to bringing new crops to the market, like cereals for food purposes and specialty crops (fruits and vegetable), whereas developers in industrialized countries are focused on the four most common field crops (**Fig. 5**). This observation confirms the data reported by previous studies about developing countries' R&D investments, which showed them to be dedicated to a broader spectrum of crop types and traits[13,14].

The pipeline of GM stacked varieties

The GM crop pipeline discussed above refers to unique, identified transformation events that are catalogued and regulated. However, a strong commercial interest exists in combining traits produced by GM technologies. Combining different traits allows the production of crops that can adapt to complex farming conditions. Furthermore, the ability to modify multiple genes within the same metabolic pathway enables metabolic engineering[15].

Combining transgenes in the same plant can be achieved by conventional breeding or by molecular tools. Commercial examples of the latter include a glyphosate-tolerant GM soybean with modified fatty acids content that has been obtained through a single transformation event with a construct harboring different transgenes, a glufosinate-tolerant and *Lepidoptera*-resistant GM maize obtained by one single transformation event with separate independent transgenes, and a GM cotton with multiple *Lepidoptera* resistance created by retransforming a cotton plant already carrying a transgene[15,16]. These cases are included in the pipeline analysis presented above because they represent unique and identified transformation events.

Of particular note, however, is the increasingly prevalent production of commercial varieties obtained through conventional breeding involving the crossing of two or more plant lines with GM events, which are commonly called hybrid or commercial 'stacks'. The growing number of authorized GM events, as previously described, provides breeders with an increasing pool of possible combinations to be stacked together. Additionally, many technology providers tend to cross-license their GM events and through this activity, many new stacks are brought to the market. Maize is the crop with most commercial stacks developed, probably due to the strong hybrid tradition in the crop[17], followed by cotton (**Fig. 6**). Up to six GM transformation events have already been combined in commercial GM maize plants.

Estimating the number and nature of commercial stacks worldwide is difficult compared with specific GM crop events because commercial stacks do not have the same regulatory treatment in all countries or regions[16]. In some jurisdictions (e.g., as the EU, Argentina, Japan, Korea and the Philippines) a commercial stack, even if it results from two authorized single GM events, requires a separate risk assessment, and therefore it is easily tracked and included in our pipeline. In other countries (e.g., Australia, Brazil, Canada, China, New Zealand, India and the United States), the need for a separate risk assessment for commercial stacks is evaluated on a case-by-case basis[4,16]. Therefore, all commercial stacks cultivated in these countries may not be represented in our pipeline analysis because there is no way to track their approval for cultivation. Thus, our pipeline likely underestimates the number and variety of stacks being cultivated worldwide. Even so, it provides an indication of how interest has been increasing in stacked GM crops, which are becoming the dominant form of GM crop grown throughout the world[1].

Global disparities in authorization and adventitious presence

GM crops have been adopted quickly in many parts of the world[1], but large disparities exist in the number of and the extent to which crops have been authorized in different countries. Most of the largest growers of GM crops are in countries that are clearly interested in exporting produce. Disparities in the GM crop authorization processes and the resulting economic impact on international trade have been described previously[5]. Other studies, mainly from industry, have also compared the time needed to obtain GM crop approval across countries[18].

An analysis of the countries in which GM events are in the commercial and precommercial stages (**Table 1**) shows that GM events of the four main field crops (cotton, maize, soybeans and oilseed rape) are cultivated in more than one country (between two and five on average), whereas other GM crops are usually cultivated in only one country. Similarly, the authorization for marketing (import) is awarded by many countries (between 8 and 15) for the main four GM crops, compared with only one for the remainder.

This disparity may be (partly) due to a delay in the authorization process of certain countries, such that additional crops will be authorized in more countries in the coming years. It may also be due to different commercialization strategies. Generally, GM crop developers request authorization for their products in those countries where commercial interest exists. In some cases, GM events have been

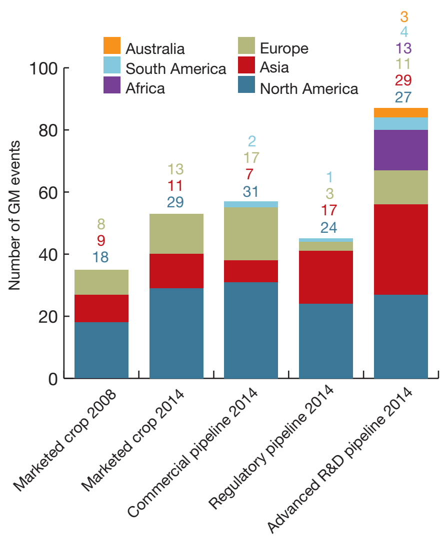

Figure 4 Distribution of GM crop developers per development phase and geographic origin.

developed only for domestic use and therefore are meant neither to be cultivated elsewhere nor to be traded. Thus, they are not submitted for authorization outside the developer's country. This tends to be more often the case for specialty crops, such as those from developing countries like China and India, than for GM events of the main field crops.

Nevertheless, it cannot be ruled out that GM crops could adventitiously end up in commercial food and feed supplies in trace amounts. According to experts, many cases of market disruptions due to the presence of unapproved GM organisms in shipments between trading partners have originated from trace amounts of GM crops from experimental field trials entering the food and feed supply chains[19]. The increasing number of GM events projected in our outlook may result in more cases of asynchronous approval or isolated foreign approvals, especially with the entry of Asian products into the pipeline.

Recently, the United Nation's Food and Agriculture Organization (FAO; Rome) reviewed the extent and pattern of trade disruptions derived from low levels of GM crops in international food and feed trade to facilitate an international dialog on this matter. In 2013, the FAO conducted an international survey to analyze the intensification of low-level GM crop presence incidents worldwide[20]. The result showed that the likelihood of these accidents is globally very high and is constantly increasing: 60 cases have been reported in eight years between 2001 and 2009 and 138 between 2009 and 2013. According to the FAO's analysis, the causes can be found in different technical and policy approaches, as well as in the high costs of the compliance measures required to minimize the risk of GM admixture, which may be unaffordable, especially for the developing countries that are gaining ground in GM crop development.

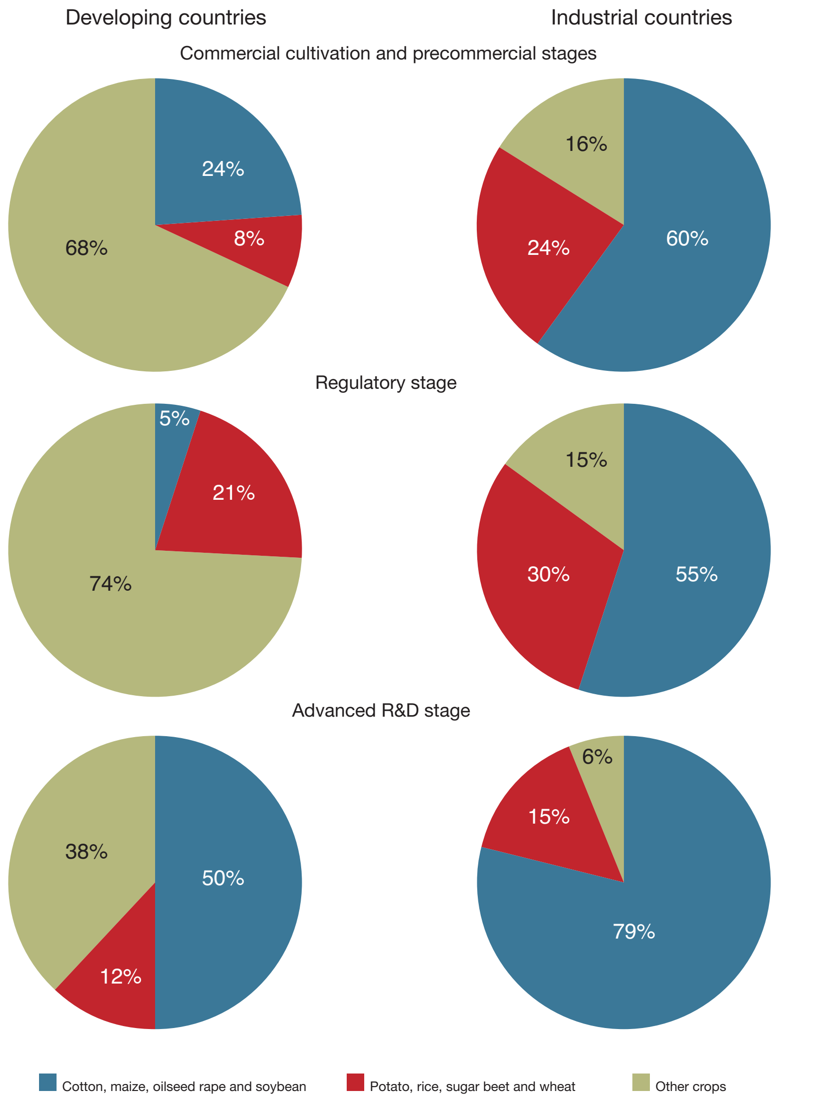

Figure 5 Distribution of type of GM crops developed at different stages in industrialized and developing countries. 'Other crops' includes, among others, banana, bean, cassava, eggplant, papaya, sugarcane and tomato. (The definition of 'developing countries' used here is that of the United Nations Development Program.)

The growth of commercial GM stacks potentially constitutes an additional cause of the low-level presence of GM crops in the EU because nonauthorized stacks, such as those produced in countries where risk assessment is not required, might end up in shipments to countries that regulate them. This risk is growing proportionately with the number of available stacks. To reduce such a risk, applicants tend to submit stack combinations with a large number of GM events to the regulatory system with the aim that their eventual authorization will imply that any lower subcombinations of the same events might also be authorized.

Conclusions

The number of GM events at the commercial cultivation, precommercial or regulatory stages has more than doubled between 2008 and 2014. Although current GM commercial varieties and the outlook for 2020 are still dominated by a few arable crops (usually for feed or industrial use) and certain agronomic traits, there is a nascent growth in quality traits, with a focus on biofortified food and industrial applications. Also, more specialty crops are being introduced into the pipeline and bean, rice, potatoes and sugarcane may be cultivated by 2020. As observed in 2008, the tendency of GM developers and breeders to combine several traits by commercial stacking continues. In fact, the number of identified commercial GM stacks is now almost equal to the number of GM events.

New technology developers are also emerging beyond the usual biotech companies, especially in developing countries like India, China, Brazil, and African developers are showing their willingness to enter the commercial field. Developing countries are showing a strong focus on a broader spectrum of crops, which could bring more specialty crops into the overall pipeline. However, so far, most of these crops have been developed mainly for domestic uses (especially in China and India).

The growing number of GM events, together with the increasing asymmetry in the authorization of GM events in different countries is causing an intensification of the low-level presence of GM crops in trade shipments worldwide. Whereas a few years ago this problem was considered a trade issue between developed economies (particularly between North and South America and the EU or Japan), it is now clearly becoming an

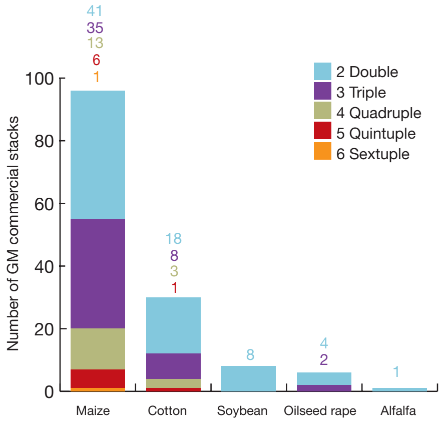

Figure 6 Number of commercial stacks identified per crop. The figure describes the data obtained in our search for multiple stacked events in the following phases: commercial cultivation, precommercial stage and regulatory stage. As explained in the **Supplementary Note**, the data mainly come from the databases of single countries' regulatory bodies and private companies' information. Because commercial stacks are regulated differently in different countries and do not need regulation in certain countries, the list is not exhaustive.

international concern that has reached the attention of the FAO. There is a strong need for an international dialog on the topic and a need for more research evaluating the global economic impact that this issue is having on the world's agricultural trade.

In addition, the number of GM crops that will be developed in the near future will be affected by the expiry of patents of broadly cultivated and exported GM crops, starting with MON810 maize (which expired in November 2014) and soybean 40-3-2 (which expired in March 2015) (ref. 21). Although this issue could potentially facilitate GM crop development by SMEs or public institutes, in practice regulatory requirements are likely to limit this possibility. In fact, once GM crop patents expire, patent owners will most likely lose the financial incentives to continue maintaining the authorized status of those crops in the countries in which the renewal authorization is required[21,22].

Finally, other factors like the technological progress in plant biotech are becoming relevant when discussing the regulation of new plant varieties. Some technological progress is still taking place within the boundaries of transgenesis, such as the use of the RNA interference technology to obtain a stable gene silencing effect, which is now applied to commercial traits including pest resistance, disease resistance[23,24] and crop composition (e.g., anti-allergy effects)[25,26].

Beyond transgenic plants, alternative methods are being applied to obtain new plant varieties[27]. New plant breeding techniques include the following: first, targeted mutagenesis with oligonucleotides or site-directed nucleases (e.g., zinc finger endonucleases, CRISPR-Cas9, or transcription activator–like effector nucleases (TALENs)); second, using transgenesis as an intermediate breeding step with the final products being free of foreign genes; and, third, employing DNA sequences only from cross-compatible plant species. The products of new plant breeding techniques are posing challenges to the national regulatory systems of different countries, due to the absence of foreign DNA sequences in the final products, despite the use of a biotech-based process. The impossibility of distinguishing these products from conventional ones using available detection methods represents an additional challenge at the regulatory level[28].

Note: Any Supplementary Information and Source Data files are available in the online version of the paper (doi:10.1038/nbt.3449).

ACKNOWLEDGMENTS

The authors wish to thank all the participants in the International Workshop on the Global Pipeline of GM crops that took place in Seville, at the JRC-IPTS (Institute for Prospective Technological Studies) premises, on June 11 and 12, 2014, for their active participation and their contribution to the description of the GM crops pipeline.

DISCLAIMER

The views expressed are purely those of the authors and may not under any circumstances be regarded as stating an official position of the European Commission.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

1. James, C. Global Status of Commercialized Biotech/GM Crops: 2014. ISAAA Brief 49. http://www.isaaa.org/resources/publications/briefs/49/default.asp (International Service for the Acquisition of Agri-Biotech Applications, Ithaca, NY, 2014).
2. Miller, J.K. & Bradford, K.J. The regulatory bottleneck for biotech specialty crops. *Nat. Biotechnol.* **28**, 1012–1014 (2010).
3. Graff, G.D., Zilberman, D. & Bennett, A.B. The contraction of agbiotech product quality innovation. *Nat. Biotechnol.* **27**, 702–704 (2009).
4. Stein, A.J. & Rodriguez-Cerezo, E. *The Global Pipeline of New GM Crops. Implications of Asynchronous Approval for International Trade* (European Commission, Joint Research Centre, 2009).
5. Stein, A.J. & Rodríguez-Cerezo, E. International trade and the global pipeline of new GM crops. *Nat. Biotechnol.* **28**, 23–25 (2010).
6. Kalaitzandonakes, N., Alston, J.M. & Bradford, K.J. Compliance costs for regulatory approval of new biotech crops. *Nat. Biotechnol.* **25**, 509–511 (2007).
7. Waltz, E. Monsanto adds dicamba to its cache to counter weed threat. *Nat. Biotechnol.* **33**, 328 (2015).
8. Cockburn, A. Commercial plant breeding: What is in the biotech pipeline? *J. Commer. Biotechnol.* **10**, 209–223 (2004).
9. De Steur, H. *et al.* Status and market potential of transgenic biofortified crops. *Nat. Biotechnol.* **33**, 25–29 (2015).
10. Wolt, J.D. & Karaman, S. Estimated environmental loads of alpha-amylase from transgenic high-amylase maize. *Biomass Bioenergy* **31**, 831–835 (2007).
11. Harwood, J.L. *et al.* Regulation and enhancement of lipid accumulation in oil crops: The use of metabolic control analysis for informed genetic manipulation. *Eur. J. Lipid Sci. Technol.* **115**, 1239–1246 (2013).
12. Falck-Zepeda, J., Gruère, G. & Sithole-Niang, I. *Genetically Modified Crops in Africa. Economic and Policy Lessons from Countries South of the Sahara* (International Food Policy Research Institute, Washington, DC, 2013).
13. Huang, J., Rozelle, S., Pray, C. & Wang, Q. Plant biotechnology in China. *Science* **295**, 674–676 (2002).
14. Atanassov, A. *et al. To Reach the Poor: Results from the ISNAR-IFPRI Next Harvest Study on Genetically Modified Crops, Public Research, and Policy Implications* (Environment and Production Technology Division, International Food Policy Research Institute, Washington, DC, 2004).
15. ISAAA. Pocket K No. 42: Stacked Traits in Biotech Crops. http://isaaa.org/resources/publications/pocketk/42/default.asp (International Service for the Acquisition of Agri-Biotech Applications, Ithaca, NY, 2013).
16. European Commission. *CO-EXTRA: GM and Non-GM Supply Chains: Their CO-EXistence and TRAceability.* Deliverable D6.4. http://bch.cbd.int/database/attachment/?id=10373 (EC, Sixth Framework Programme, 2008).
17. De Schrijver, A. *et al.* Risk assessment of GM stacked events obtained from crosses between GM events. *Trends Food Sci. Technol.* **18**, 101–109 (2007).
18. EuropaBio. *Approvals of GMOs in the European Union* (European Association of Bioindustries, Brussels; 2011).
19. Kalaitzandonakes, N., Kaufman, J. & Miller, D. Potential economic impacts of zero thresholds for unapproved GMOs: the EU case. *Food Policy* **45**, 146–157 (2014).
20. FAO. Technical Consultation on Low Levels of GM Crops in International Food and Feed Trade. Food and Agriculture Organization of the United Nations. Rome, Italy, 20–21 March 2014. http://www.fao.org/food/food-safety-quality/a-z-index/biotechnology/LLP/en/
21. Grushkin, D. Threat to global GM soybean access as patent nears expiry. *Nat. Biotechnol.* **31**, 10–11 (2013).
22. Conko, G. Is There a Future for generic Biotech Crops? Regulatory Reform is Needed for a Viable Post-Patent Industry. Issue Analysis 2012 No. 7. (Competitive Enterprise Institute, 2012).
23. Koch, A. *et al.* Host-induced gene silencing of cytochrome P450 lanosterol C14α-demethylase-encoding genes confers strong resistance to Fusarium species. *Proc. Natl. Acad. Sci. USA* **110**, 19324–19329 (2013).
24. Mao, Y.-B., Tao, X.-Y., Xue, X.-Y., Wang, L.-J. & Chen, X.-Y. Cotton plants expressing CYP6AE14 double-stranded RNA show enhanced resistance to bollworms. *Transgenic Res.* **20**, 665–673 (2011).
25. Gil-Humanes, J., Pistón, F., Tollefsen, S., Sollid, L.M. & Barro, F. Effective shutdown in the expression of celiac disease-related wheat gliadin T-cell epitopes by RNA interference. *Proc. Natl. Acad. Sci. USA* **107**, 17023–17028 (2010).
26. Dodo, H.W., Konan, K.N., Chen, F.C., Egnin, M. & Viquez, O.M. Alleviating peanut allergy using genetic engineering: the silencing of the immunodominant allergen Ara h 2 leads to its significant reduction and a decrease in peanut allergenicity. *Plant Biotechnol. J.* **6**, 135–145 (2008).
27. Lusser, M., Parisi, C., Plan, D. & Rodríguez-Cerezo, E. Deployment of new biotechnologies in plant breeding. *Nat. Biotechnol.* **30**, 231–239 (2012).
28. Lusser, M., Parisi, C., Plan, D. & Rodríguez-Cerezo, E. New Plant Breeding Techniques. State-of-the-Art and Prospects for Commercial Development. JRC Technical Report EUR 24760 EN. (European Commission. Joint Research Centre, 2011).