GMO FIELD TRIALS IN EUROPE AND WORLDWIDE - ASSESSMENT OF PROGRESS AGAINST PREDICTIONS AND POSSIBLE FUTURE DEVELOPMENTS

1. GMO FIELD TRIALS IN EUROPE

1.1 Introduction

In future years the EU is likely to witness a host of innovative solutions to crop management, crop protection, yield improvement and many other diverse agricultural and consumer needs. Some of these may be provided by genetic modification, which remains at the cutting-edge of agricultural biotechnology. In the face of these new developments biotechnology regulators need to be confident that the legislative systems in place are satisfactorily robust to protect human health and the environment and inspire public confidence, whilst still remaining supportive of these new technologies. Regulators need to gain insight into future developments in GM crops and traits to enable them to assess whether current legislation is fit for purpose, or whether amendments may be needed, to ensure timely policy responses. In the case of Directive 2001/18/EC, the early identification of any new GM crops and traits that are on the horizon is a useful step in determining the suitability of the legislation for future years. In order to enhance regulatory foresight in this area a review of GMOs under research and development was published by Lheureux *et al.* in 2003, with the aim of identifying and characterising future waves of GMO development. This document, which was commissioned by the Directorate-General Agriculture (DG AGRI), provides a useful reference source from which to compare predicted developments of GM crops and traits with actual developments, as documented in the JRC database of Part B notifications[1]. In the sections that follow, the actual development of GMOs in Europe is compared with the developments predicted by Lheureux *et al*. Developments in the USA, Canada and multi-national companies are then reviewed to give a view of what might be entering EU GMO field trials up to 2018.

1.2 Number of notifications

Since 1991 there have been a total of 2244 Part B deliberate release (DR) notifications of GMO field trials in the EU. Of these, 1813 were submitted under Council Directive 90/220/EEC[2] and 431[3] were submitted under Directive 2001/18/EC[4]. Figure 1 shows the number of notifications submitted per year. Notifications put forward by the fifteen MSs making up the EU prior to 2004 are shown in green. Between 1991 and 1996 it can be seen that there was a steady increase in the number of Part B notifications, culminating in a peak of 264 notifications in 1997. After 1998 the number of notifications decreased quite dramatically[5] reaching a low of just 56 notifications in 2002. Since 2002, however, there has been a gradual increase in the number of notifications, up to 111 in 2007,

1 Data for the actual development of GMOs has been obtained from notifications posted on the JRC website. It should be noted that these notifications represent applications for Part B trials. As such they may be subject to subsequent amendment or cancellation (e.g. by the Competent Authority) or withdrawal (by the notifier). Despite these limitations, notifications provide a useful source of information on the types of plants and traits that are being put forward for field-testing in the EU, and the proposed conditions which attend these applications.

2 Council Directive of 23 April 1990 on the deliberate release into the environment of genetically modified organisms [repealed on 17/10/02].

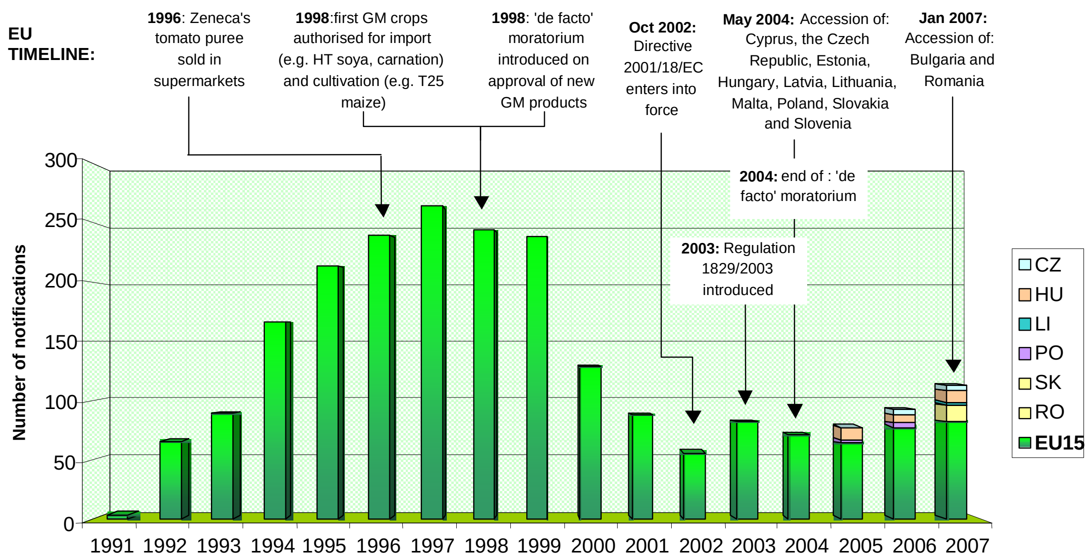
3 Based on data available on the JRC website up to the end of December 2007.

4 Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.

5 A decrease of 76% from 1998 to 2001, as noted by Lheureux et al. 2003. Note: 2001 was the last year for which the authors had complete data.

although it is worth noting that a proportion of this increase is due to the accession of new Member States, such as the Czech Republic, Hungary, Poland, Lithuania and the Slovak Republic in 2004 (accounting for a total of 44 notifications between 2005 and 2007), and Romania in 2007 (accounting for 14 notifications). Notifications put forward by the new member states are shown using separate colours (see graph legend).

Figure 1: Annual number of field trial notifications in the EU between 1991 and 2007 (based on data from the JRC SNIF database)[6]



It would not be unreasonable to expect that, as new MSs joined the EU, notifiers turned towards these countries when submitting new deliberate release applications, either increasing the overall number of applications, or reducing the number of Part B trials in 'older' MSs. Table 1 compares the number of notifications received by the new MSs compared to the average from the original 15 EU countries (EU15). In 2005, following the accession of the 10 new MSs, an average of 4.3 notifications per MS were submitted to the CAs of the 'EU15' countries, and an average of only 1.4 notifications were submitted to the new MSs (as this is an average it must be appreciated that there is quite wide variation between individual MSs. Hungary for example, has received 26 notifications between 2004 and 2007, whereas other MS have received none). 2007 was the year in which Romania and Bulgaria joined the EU, and of note is the relatively large number of notifications submitted to Romania. Given the amount of variability in notifications submitted to MSs, it is probably too early to confirm if there is an actual trend, although it does appear that some of the new MSs, most notably Hungary and Romania have the potential to attract a large number of notifications.

[6] SNIF: Summary notification information format.

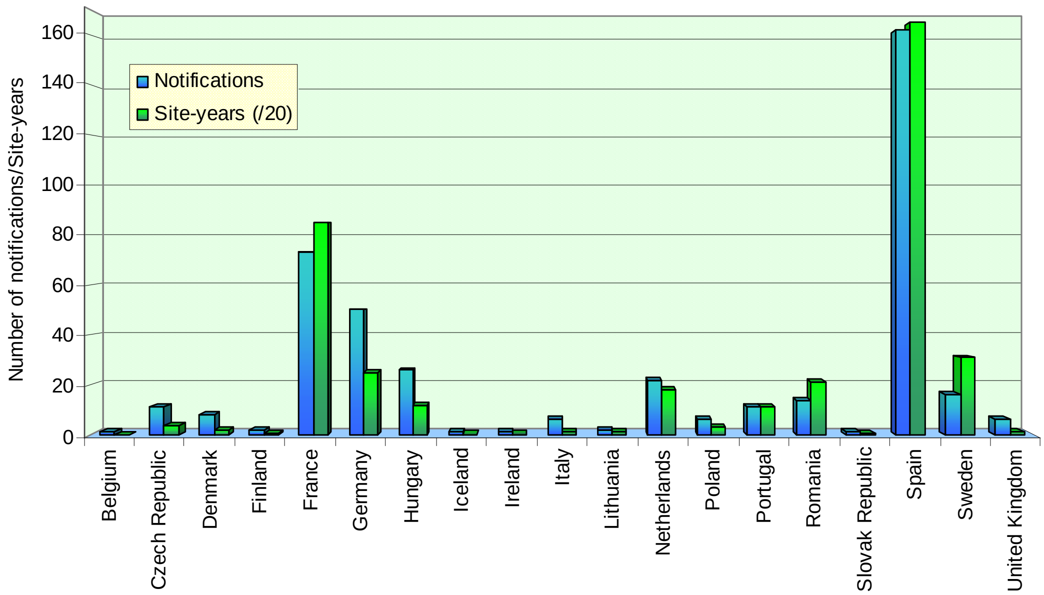
Table 1: Number of notifications received by existing and new MS between 2004 and 2007

Year	EU15 (average)	MS that joined the EU in 2004							MS that joined in 2007		
		CZ	HU	PL	LT	SK	CY, EE, LV, MT, SI[1]	EU10 (average)	RO	BG	EU2 (average)
2004	4.8	-	-	-	-	-	-	-	-	-	-
2005	4.3	1	10	3	-	-	-	1.4	-	-	-
2006	5.2	5	7	3	-	-	-	1.5	-	-	-
2007	5.5	5	9	-	2	1	-	1.7	14	-	7.0

[1] Cyprus, Estonia, Latvia, Malta and Slovenia have not received any Part B notifications and are grouped together for this reason.

Figure 2 shows Part B trials activity according to MS, with the blue bars showing the number of Part B notifications submitted to each MS under 2001/18/EC. It can be seen that Spain has recorded the highest number of notifications at 162, followed by France with 73, Germany with 50, Hungary with 26 and the Netherlands with 22. Number of notifications may not, however, be the best indicator of GM trials activity, because each notification can cover a number of years as well as a number of release sites (the average duration of EU Part B notifications is approximately 3.8 years; the average number of sites per notification is 5.8). Those MS that have a predominance of short-timescale trials with low numbers of release sites per notification will be over-represented compared to MSs which have trials extending over several years and/or utilizing several release sites. The number of 'site-years' may, therefore, be a better indicator of Part B activity. Site-years are calculated by multiplying the number of years' duration with the number of release sites for each notification, and adding these together to obtain a total for each MS (an example of calculating site-years can be found in Appendix 12). In figure 2 and in table 2, site-years are represented by the green bars: for most MS there appears to be a high degree of correlation between site-years and the number of notifications.

Figure 2: Number of Part B notifications submitted under 2001/18/EC, according to Member State



[1] *A scaling function (i.e. division by 20) was applied to the number of site-years for each MS in order to fit on the same axis as the number of notifications.*

The data suggests that notifications submitted to France and Romania generally contain a greater number of release sites per notification than the EU average, and those submitted to Sweden generally have a longer time-span as well as a somewhat larger than average number of sites. Conversely, notifications submitted to Germany contain, on average, fewer release sites, and in the case of Hungary both the number of years and number of sites per notification are below the EU average. The reason for these differences is not immediately obvious; it might be expected, for example, that MS hosting a large number of trials involving slow-growing or slow-to-mature species (e.g. trees such as poplar (France) or birch (Finland)) may require longer timescales, but this is not borne out by the data.

Table 2: Number of notifications and 'site-years' received by each MS

	Total number of notifications	Total number of years	Total number of trial sites	**Number of 'site-years'**
Belgium	1	4	1	4
Czech Republic	11	48	19	74
Denmark	8	30	9	35
Finland	2	9	2	9
France	73	259	545	1701
Germany	50	217	115	500
Hungary	26	96	63	240
Iceland	1	6	1	6
Ireland	1	5	1	5
Italy	6	20	6	20
Lithuania	2	10	4	20
Netherlands	22	105	50	362
Poland	6	28	17	60
Portugal	11	43	57	226
Romania	14	63	81	424
Slovak Republic	1	3	4	12
Spain	162	386	1409	3297
Sweden	16	125	125	621
United Kingdom	6	18	7	23

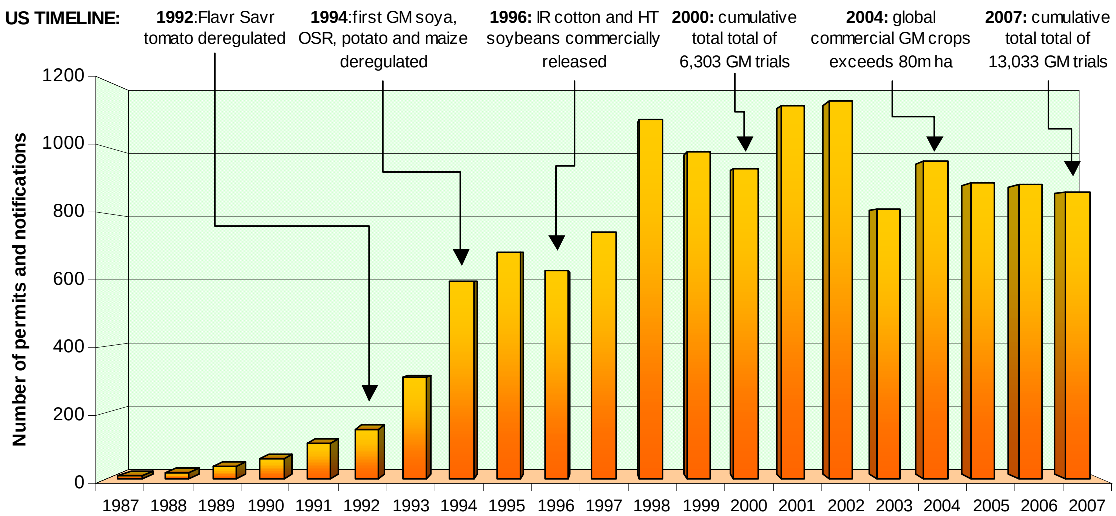
- *Comparison with numbers of field trials in the USA*

The country that has conducted the most GM trials, from a global perspective, is the USA, and some observers believe that trends in that country can be used as a barometer for future EU trends, at least in a broad sense. By way of comparison with the EU, there have been 13,032 GM field test notifications[7] in the USA since 1987 (APHIS 2007), when GM trials first commenced in that country. Although it is not possible to make a direct comparison between EU and US notifications due to differences in how the data are collected (for example, the US system requires a notification for every year, whilst some EU notifications can cover a number of years[8]), it is possible to make some broad comparisons. As can be seen in figure 3, an exponential growth in the number of US notifications occurred in the early years of biotechnology development (1987 to 1994), with a peak between 1998 and 2002 (reaching a maximum of 1141 notifications in 2002). Since then there has been a slight decline, resulting in 867 notifications in 2007 (the most recent data available). Interestingly, from 2004 onwards EU notifications have increased whilst US ones have decreased slightly.

[7] Consisting of both 'permits' and 'notifications' (for a definition of these terms see the section on the USA regulatory system in Section 6

[8] Spain requires annual notifications

Figure 3: Total number of US GMO trial permits & notifications approved by year.

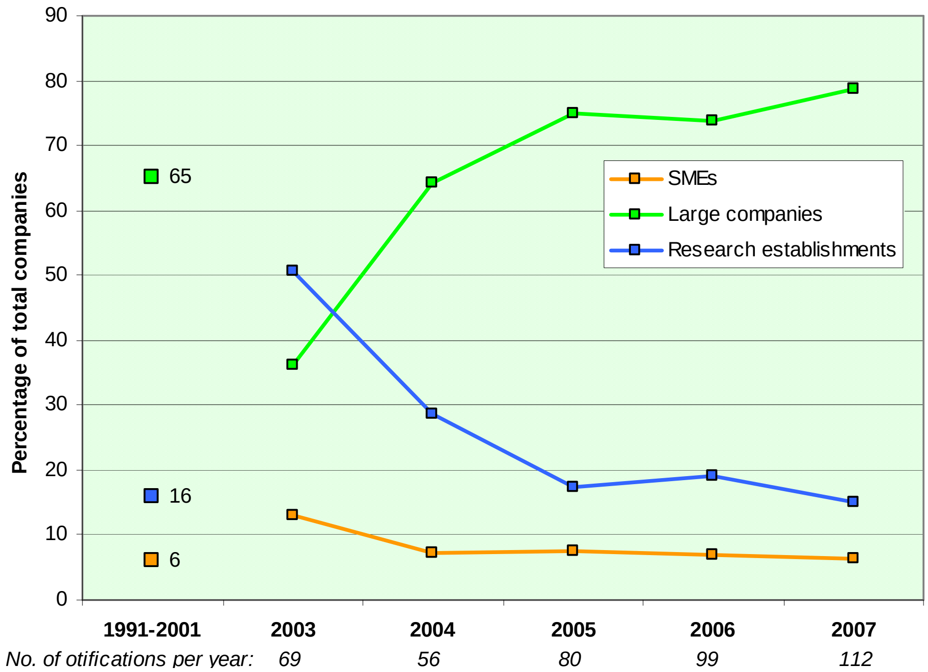


1.3 Types of companies placing notifications in Europe

The types of companies involved in GMO field trials can largely be divided into three types, comprising large companies, small-medium sized enterprises (SMEs), and research establishments[9]. By examining changes in the relative ratios of these three groups over time, in terms of field trials activity, it may be possible to gain an insight into the functioning of the regulatory system as a whole. Figure 4 shows the changing ratios of the various types of company submitting Part B notifications, over time. Between 1991 and 2001 approximately 65% of all field trials notifications were submitted by large companies, with 6% submitted by SMEs and 16% submitted by research establishments (Lheureux *et al.,* 2003), as shown by the isolated points on the graph. Each of the data points for 1991-2001 represents an average, therefore it is not possible to say whether the data show a trend. However, since the introduction of 2001/18/EC the number of notifications submitted by large companies has increased fairly dramatically over time, from around 35% in 2003 to almost 80% of notifications in 2007. Conversely, the number of notifications submitted by research institutes has declined considerably over the same period, from around 50% in 2002 to just 15% in 2007. Likewise, the number of notifications submitted by SMEs, has also decreased, although this number was initially very low.

[9] 'Large companies' are classed as those with more than 500 employees; 'SMEs' (small to medium enterprises) are those with less than 500 employees; 'Research establishments' include public research institutes, universities, and the like. Please note this is based on our own assessment of notifiers, not an official classification.

Figure 4: Types of companies submitting Part B notifications



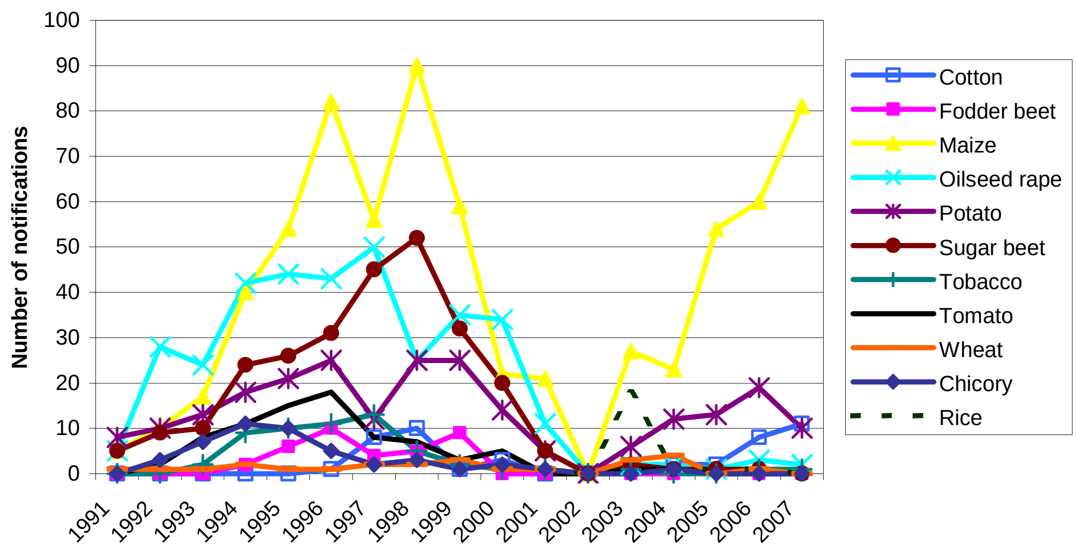
Note: 2002 is not shown as no notifications were received under 2001/18/EC for this year.

There are a number of possible explanations for the changes shown in figure 4. The reduction in the number of notifications submitted by research establishments and smaller companies may be due to increasing costs involved in trialling GMOs and/or bringing products to market. This could be due to the increasing costs of managing trials (e.g. personnel costs, land leasing, equipment hire, etc.). Alternatively, the decline in the number of notifications submitted by SMEs may reflect the current public scepticism towards GMOs, with smaller companies unable to see sufficient monetary returns in order to invest in this type of technology. The decline in notifications from research establishments may simply be due to a shift in the emphasis of research work, as GM technology becomes less of a cutting edge science. This decline could also be interpreted as being due to the prohibitive costs imposed by some aspects of the legislation (e.g. the time and effort required to prepare notifications, managing the trials, or fulfilling monitoring requirements). We also know from the survey of MS in this study, that many trials have suffered vandalism and have been terminated, and smaller companies may find it more difficult to absorb the cost of such actions, or to put measures in place to try to prevent it happening. The outcome of this may be that as time progresses only large multi-national companies will be able to finance the cost of Part B release trials.

1.4 Types of crops

There are a wide variety of crop types that have been the subject of EU Part B trials notifications (32 different species in total), ranging from ‘model’ plants such as *Arabidopsis thaliana* used to study particular biological phenomena, to widely utilised food/feed crop plants such as maize, soya and potatoes. The dominant plant species in terms of Part B notifications are oilseed rape, maize, sugar beet and potato, which have been at the forefront of notifications since trials began in the early 1990s. In those early years (1991-1994), oilseed rape was the dominant GMO in trials, but in 1995 this was surpassed by maize, which rose to a peak of 90 notifications in 1998 (figure 5). The other major GM crops between 1991 and 2001 were sugar beet and potato, peaking at 52 and 25 notifications respectively.

Figure 5: Type of GM crops in EU field trials between 1991 and 2007 (based on data from the JRC)



GM crops with lower numbers of notifications between 1991 and 2001 were tomato, cotton, fodder beet, chicory and wheat. After 1999 there was a marked drop in the number of notifications generally, culminating in a hiatus of approvals in 2002, possibly due to the implementation (in 1999) of the *de facto* moratorium on any new authorisations for marketing GM crops. There may also have been some uncertainty or unfamiliarity relating to the implementation of Directive 2001/18/EC that contributed to the drop in notifications. As already stated, the number of notifications reached its lowest point in 2002: the EU SNIF database lists 56 notifications with trials commencing in 2002, but further analysis shows none of these were submitted under 2001/18/EC (i.e. they were submitted under 90/220/EEC). Since 2002 there has been a rise in the number of notifications, with maize in particular increasing rapidly, up to 81 notifications in 2007 (though still not as high as the 1999 peak). Potato has shown a relatively steady rise in the number of notifications, peaking at 19 in 2006, although again numbers are not a high as pre-2000 levels. Furthermore, 2007 (the latest year for which results are available) saw a drop in potato notifications. This may be due to the fact that the altered starch potato (Amylogene C/SE/96/3501) is approaching commercialisation, and the majority of environmental and agronomic data has been collected. In 2003 GM rice saw an increase in field trials activity (8 notifications, all submitted to Spain), but since then there have been no further applications.

Figure 6, below, shows the percentage of field trial notifications in terms of crop types between the periods 1991 and 2001 and 2001 and 2007. As can be seen, in the years 1991 to 2001 maize was the dominant crop in Part B trials, making up around 26% of notifications. In the period 2001 to 2007 this share has almost doubled to over 57% of all notifications. Between 1991 and 2001 oilseed rape was the next most prolific crop in terms of notifications, at 21%, followed by potato at 11%. However, whilst potato notifications have increased to almost 15%, oilseed rape notifications have dwindled to just 3% in the period 2001 to 2007. Similarly, sugar beet accounted for 15.6% of notifications between 1991 and 2001, shrinking to just 1.2% between 2001 and 2007.

Figure 6: Distribution of crops in GMO field trial notifications submitted under 90/220/EEC (1991 – 2001) and 2001/18/EC (2001 up to 2007)

Chart 1: 1991 – 2001[1]

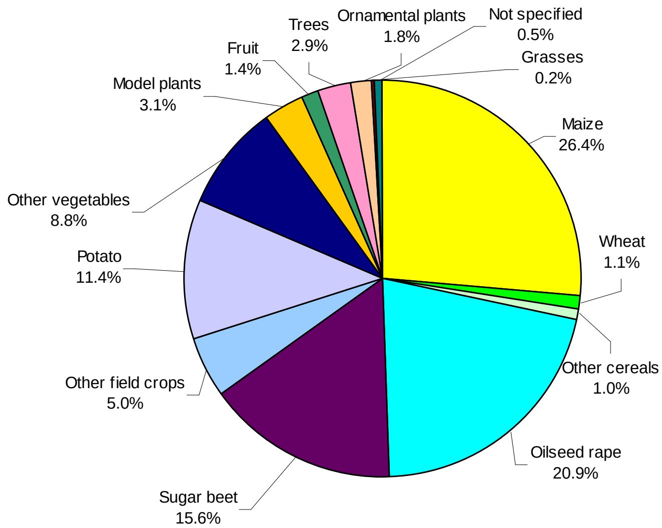
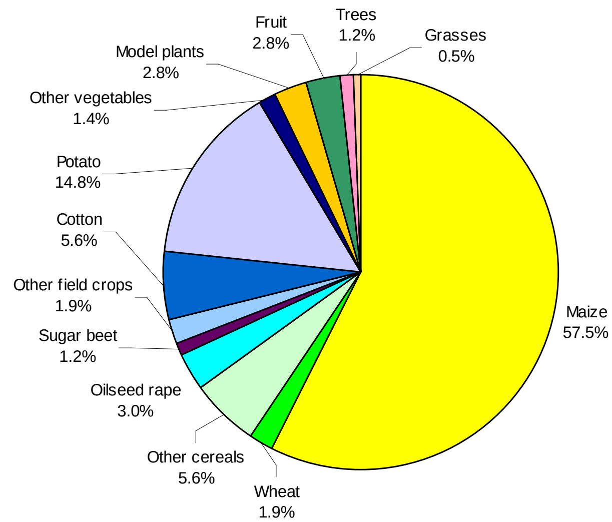


Chart 2: 2001 - 2007



Notes:
'Other cereals' include barley, buckwheat, rice and triticale;
'Other field crops' include coffee, cowpea, soybean, fodder beet, linseed and chicory;
'Fruit' includes apple, pear, grape, lemon, plum;
'Model plants' include *Arabidopsis thaliana*, tobacco, *Solanum nigrum*;
'Other vegetables' include asparagus, aubergine, broccoli, cabbage, carrot and tomato;
'Trees' include birch and poplar.

Of the less prevalent GM crops, notifications for ‘other cereals’ have increased from 1% in 1991-2001 to almost 6% in the period 2001-2007, and notifications for ‘other field crops’ now account for 7.5% of notifications, up slightly from 5.0%. ‘Fruit ‘ crop notifications have doubled from 1.4% to 2.8%, ‘Grasses’ have increased from 0.2% to 0.5% (more than doubling the number of notifications), whilst ‘model plants’ have remained fairly static at around 3%. Notifications for GM vegetables have decreased considerably, from 8.8% to 1.4% and the number of notifications for trees have more than halved, from 2.9% to 1.2%.

Also of note is the fact that the number of different plant species featured in Part B trials appears to have declined substantially over the years that the Directive has been in operation. Historical data from the JRC website shows that 68 different plant species featured in notifications since the implementation of Directive 90/220/EEC (21 October 1991). Data from notifications submitted under 2001/18/EC reveal the presence of just 31 plant species, a reduction of over 50% (see Appendix 12).

Overall it appears to be that notifiers are concentrating on the more established GM traits (herbicide tolerance, insect resistance and altered starch) and focussing on the ‘big’ agricultural crops (i.e. maize, cotton and potato), where there is already a precedent for commercialisation. These ‘major’ GM crop types are destined either for animal feed (i.e. maize) or industrial uses (i.e. cotton and potato), and there appears to be a distinct move away from GM crops for human consumption, such as vegetables (aubergine, broccoli, cabbage, etc.) and other cereals (wheat, barley, triticale etc). This is possibly due, at least in part, to the lack of public enthusiasm for GM crops. In addition, maize, cotton and potato are perhaps less controversial than many GM crops in that there are few, if any, closely related species in the EU[10,] hence the risk of gene flow to wild relatives is much less of an issue than for GM crops such as oilseed rape or fodder/sugar beet.

1.5 Types of traits

Lheureux *et al.* define GM traits as either input traits or output traits:

- ‘Input’ traits provide an agronomic advantage to the crop or plant, and include herbicide tolerance, insect resistance, resistance to other pathogens (including fungi, bacteria, virus, other species), abiotic stress/yield characteristics and male sterility.
- ‘Output’ traits enhance the quality of the final GM product, and include modified nutrients/ingredients, products for industrial use and health-related ingredients (molecular farming).

In 2003 Lheureux *et al*. noted that input traits were more prevalent than output traits (77% vs. 19% respectively), and suggested the reason for this was that output traits were still in an early phase of research, as well as possible technical and economic reasons associated with them (due to the high cost of production and identity

[10] **Maize**: no wild relatives in Europe, making out-crossing with naturally occurring plants little cause for concern; **Potato**: the movement of genes to wild species is extremely unlikely as potatoes reproduce by way of tubers and any pollination will not affect the makeup of the plant’s tubers and therefore is not passed on to future generations. It is theoretically possible that some transgenic seeds could be produced from cross-pollination events, but potato seeds, as a general rule, do not survive under field conditions. Although wild relatives of potatoes do exist in Europe, none of them are understood to be sexually compatible under field conditions; Cotton: the origin of the genus **Gossypium** is unknown, but the genus' primary centres of diversity are Mexico, Africa, Arabia, and Australia. No members of the Gossypiaea family are native to the EU.

preservation). An assessment of current notification data (table 3) shows that, rather than narrowing, this discrepancy between input and output traits has actually widened (86% vs. 12% respectively), with a higher proportion of notifications for agronomic traits than for quality traits.

Table 3: Proportion of input and output traits 2001-2007

Input traits	Percentage
Abiotic stress resistance	2
Herbicide tolerance	43
Insect resistance	33
Pathogen resistance	6
Increased starch, oil, general yield, etc.	3
subtotal	*85*
Output traits	
Altered oils, starch, etc	8
Altered development	2
Modified consumer properties	2
Industrial use/molecular farming	<1
subtotal	*12*

Lheureux *et al*. commented on the fact that health-related compounds were almost absent from EU field trials notifications, and contrasted this with the laboratory R&D phase, where 11% of projects involved molecular farming traits. The lack of trials was ascribed to the fact that this area of research was at an early stage of development, however, there are still only a small number of notifications relating to molecular farming, which may indicate a lack of progress in this area or a high level of caution.

Also of note is the increasing number of notifications with stacked events, including multiple herbicide tolerance and multiple insect resistance[11]. In 2003, despite the low numbers of notifications submitted at the time, Lheureux *et al*. also noted an increase in stacking following the implementation of 2001/18/EC, specifically: “At the time of writing (March 2003), a total 19 applications have been submitted according to the provisions of the new Directive. These applications … do not represent drastic changes (regarding species and traits) to the types of GM plants described above, but there is a significant increase in the presence of GM plants with stacked traits”.

Under 90/220/EEC, almost 34% of the notifications referred to two stacked traits and over 8% referred to three stacked traits[12], with the most common combinations being input traits, such as herbicide tolerance/insect resistance in maize, herbicide tolerance/male sterility in oilseed rape, and herbicide tolerance/virus resistance in sugar beet. Between 2001 and 2007 the number of notifications with stacked traits increased to 43% of the 431 notifications registered. Table 4 shows the distribution of these, hence maize now accounts for 86.5% of stacked traits, cotton accounts for 6.5%, with a diverse array of other species making up the remaining 7%.

[11] A trait used simply as marker gene is not regarded as a “stacked” trait.
[12] In older notifications, when several traits are mentioned, this may refer either to stacked genes or to several independent GMOs. Recent notifications, under 2001/18/EC, are much more likely to refer to a single GMO.

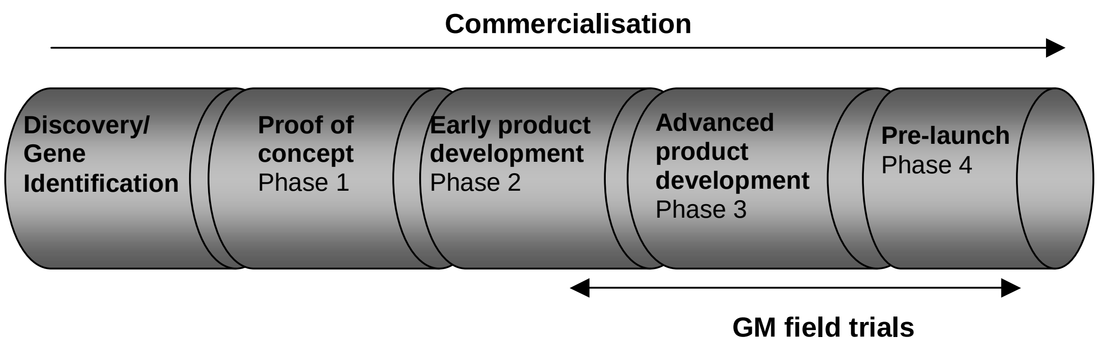
Table 4: Number of notifications with stacked traits submitted under 2001/18/EC

Species	Notifications	Percentage	Stacked traits
Maize	160	86.5	Insect resistance/herbicide tolerance/abiotic stress resistance/altered product/enhanced yield (up to 4 stacked traits)
Cotton	12	6.5	Insect resistance / herbicide tolerance
Potato	3	1.6	Altered/increased starch / fungal resistance / enhanced functional ingredients / altered carbohydrate composition
Rice	3	1.6	Salinity tolerance/drought tolerance
Linseed/flax	2	1.1	Herbicide tolerance, fungal resistance and insect resistance / industrial/chemical products and enhanced functional ingredients
Apple	1	0.5	Fungal & bacterial resistance
Grape	1	0.5	Insect resistance / herbicide tolerance
OSR	1	0.5	Herbicide tolerance/altered pollination control
Sugar beet	1	0.5	Herbicide tolerance / virus resistance
Tall fescue	1	0.5	Herbicide tolerance / altered lignin
Total:	**185**	**100%**	**(Data for 2001-2007)**

1.6 Future crops and traits

Product development of GM crops, commonly referred to as ‘pipelines’, is influenced by many factors, including the crop, complexity of the trait, the type of product, business factors including licensing and intellectual property (IP) and regulatory regimes (Glover et al, 2005). Generally companies refer to four or five phases of trait development. These are gene discovery, proof of concept, early product development, advanced product development and pre-launch (figure 7). Some companies amalgamate the advanced product development and pre-launch phases. Field trials start in the early phase of product development and progress through to the pre-launch phase. The time span from initial discovery to commercialisation varies between companies but in the USA is thought to take between 8 to 12 years (Gutterson and Zhang, 2004).

Figure 7: Typical development phases for GM crops (after Casale, 2008)

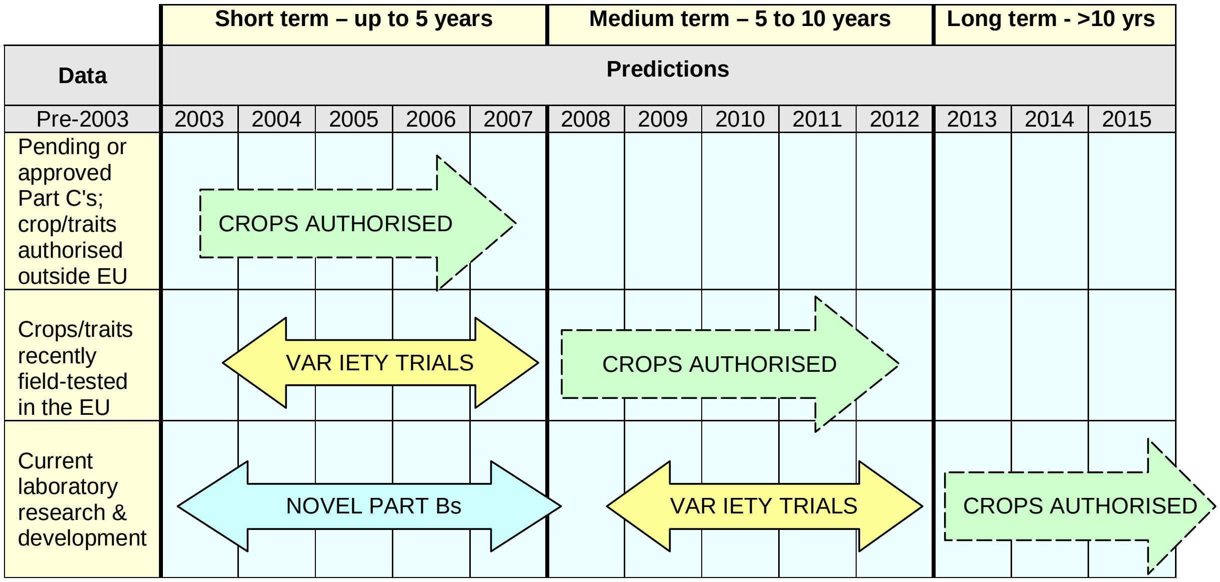


As already stated, the aim of the 2003 study by Lheureux *et al*., was to try to determine which agricultural GM plants are most likely to be developed up to the market level in future years. The authors identified a number of “pipeline” lists showing the types of GM plants and GM traits that were predicted to appear in the future. Specifically, the lists were aimed at flagging-up those GM plants most likely to request authorisation for marketing in the EU for cultivation and/or import within a specified time period[13]. These lists are divided into short term (next 5 years), medium term (next 5 to 10 years) and long term (beyond 10 years) perspectives[14]. Figure 8 is a graphical representation of the rationale used by Lheureux *et al*., and illustrates the predicted timescales for the development and authorisation of GM crops in the EU. The first column summarises the 2002 information that Lheureux *et al*. based their marketing predictions upon, with the expected authorisation periods shown by the green arrows.

[13] Under Part C of the Directive, Placing on the market of GMOS as or in products.

[14] Assuming that the study information was obtained in 2002, “the next 5 years” corresponds to 2003 – 2007, “the next 5 to 10 years” corresponds to 2007-12, and “beyond 10 years” corresponds to 2012 and beyond.

Figure 8: Rationale and anticipated timeline behind the predicted development of GMO plants



Notes: The first column ('Data') shows the pre-2003 information that Lheureux *et al*. based their marketing predictions upon (i.e. pending or approved Part Cs for short term predictions; recent EU field-tests for medium term predictions; contained-use research and development for long term predictions).

As already stated, it takes between 8 and 12 years to develop a new GM crop variety, including 5 to 6 years of field trials research; hence if Lheureux's predictions regarding authorisation are correct it should be possible to calculate the expected timescales for variety registration trials (represented by the yellow arrows) and novel Part B releases (represented by the blue arrows). So, for example, crops pending approval in 2002 would be expected to be authorised in the period 2003 to 2007[15]; crops that were field tested in the period up to and including 2002 would be expected to be present in Part B variety registration trials between 2003 and 2007 (with a greater number of such notifications as the crop approaches commercialisation); and crops featured in laboratory research and development work up to and including 2002 would be expected to be present as novel plants in Part B trials between 2003 and 2007. Thus, although we only have data up to and including 2007, it should be possible to determine the validity of the Lheureux *et al.* predictions by comparing their pipeline lists with current Part C and Part B releases. Furthermore, it should be possible to determine the reliability of the method in predicting future novel GM crops, although the further into the future you try to look, the less accurate your predictions are likely to be.

1.7 'Short term' pipeline GM products: predictions for 2003 - 2007

Lheureux *et al*. predicted a 'short term' pipeline list based on GMOs that were pending authorisation in Europe (or had already been approved for commercialisation) and on GM plants approved in the main GMO growing countries (i.e. US, Canada, Argentina). This list is shown in the first column of table 5, below.

[15] Although this is, of course, a simplification of matters, due to the hiatus of GMO approvals from 1998 to 2004, the introduction of food and feed legislation (Regulation (EC) No 1829/2003 on genetically modified food and feed), and the fact that some applications will be rejected or withdrawn.

Table 5: Comparison of predicted and actual 'pipeline products' for 2003 – 2007.

Commercialisation predicted 2003 – 2007	**Actual** (products on market 2003 – 2007[a]) (crops shown in **bold** indicate where commercialisation has been achieved)
Herbicide tolerant: • maize • oilseed rape • soybean • wheat • sugar beet • fodder beet • cotton • chicory	 • **maize – 3 lines** (GA21, T25, NK603) • **oilseed rape - 6 lines** (T45, MS8xRF3, GT73, MS1xRF2, MS1xRF1, Topas 19/2) • **soybean – 1 line** (MON 40-3-2) • wheat - none • **sugar beet – 1 line** (H7-1) • fodder beet - none • **cotton – 1 line** (Mon 1445) • chicory – none
Insect-resistant: • maize • cotton • potatoes	 • **maize – 5 lines** (Bt11, Bt176, MON810, MON863, MON863xMON810) • **cotton – 2 lines** (MON 15985, MON 531) • potatoes – none
Modified starch or fatty acid content in: • potatoes • soybean • oilseed rape	 • **potatoes – 1 line** [EH92-527-1 is currently **pending approval**] • soybean - none • oilseed rape – none
Modified colour/form: • flowers	 • **carnation – 3 lines** (Moonlite, Moonshadow 1, Moondust)
Modified fruit ripening: • tomato	 • tomato – 1 line
Herbicide tolerant and insect-resistant: • maize • cotton	 • **maize – 6 lines** (1507, 59122, 1507xNK603, GA21xMON810, MON863xNK603, NK603xMON810) • **cotton – 2 lines** (MON15985xMON1445, MON531xMON1445)
Products NOT PREDICTED but PRESENT on the market 2003-2007:	• **carnation – 1 line** (Moonshadow 2 - increased shelf-life) • **rice – 1 line** [herbicide tolerant LL RICE 62 is currently **pending approval**]

[a] marketing includes cultivation, import and processing, and food and feed.
Note: the above table includes lines authorised under 2001/18/EC, those previously authorised under 90/220/EEC, and those authorised under 1829/2003.

If the predictions of Lheureux *et al*. proved to be correct, then the crops featured in this short-term pipeline list would be expected to be on the market by 2007. Column 2 of table 5 shows the actual situation (2003 to 2007) in terms of Part C notifications, and reveals that many of the predictions have been realised. Crops such as herbicide tolerant maize, oilseed rape, soya and sugar beet have all been cleared for marketing, either for cultivation or for food and feed use (Lheureux's predictions were not specific in terms of usage). Similarly, marketing status has been granted for insect resistant maize and cotton, and is currently pending for modified starch potato. Carnations with modified flower colour have had marketing consent since 1996, and the stacked traits of herbicide tolerance and insect resistance have been authorised in both maize and cotton, as predicted.

Where Lheureux's predictions have failed to be realised is in the case of herbicide tolerant wheat, fodder beet, and chicory, insect resistant potatoes, modified starch or modified fatty acid content in soya and oilseed rape, and modified fruit ripening in tomato. In addition, marketing consent has been granted for flowers with increased shelf life, and is pending for herbicide tolerant rice.

1.8 'Medium term' pipeline GM products: predictions for 2008 - 2012

The first column of table 6 shows the medium term 'pipeline list' of GM products predicted by Lheureux *et al*., which equates to commercialisation over the timescale 2008-2012. Whilst it is too early to say whether these predictions are correct, it is possible to obtain a good indication of this by assessing how far the crops have progressed along the regulatory pathway to date. Crops predicted to be approaching marketability in 2008-2012 would be expected to be in Part B variety registration trials during the period 2003-2007. Crops in variety registration trials are shown in bold in column 2. Information in square brackets shows the number of notifications for releases other than variety registration purposes. Years shown in brackets indicate the overall period of release of the trials(s).

Table 6: Comparison of predicted and actual 'pipeline products' for 2008 - 2012

Commercialisation predicted 2008 - 2012	**Actual** (GM variety registration trials 2003 – 2007) (crops shown in **bold** indicate where variety registration trials have taken place)
Fungi-resistant: • Wheat • Oilseed rape • Sunflower • Fruit trees	*Fungi-resistant:* • Wheat – none [5 agronomic/efficacy notifications] • Oilseed rape – none • Sunflower - none • Fruit trees – none [3 apple agronomic/environmental assessment; 1 lemon agronomic/efficacy/environmental assessment]
Virus-resistant: • Sugar beet • Potato • Tomato • Melon • Fruit trees	*Virus-resistant:* • Sugar beet – none [4 agronomic/efficacy assessment] • Potato – none • Tomato - none • Melon - none • Fruit trees – none
Herbicide-tolerant: • Wheat • Barley • Rice	*Herbicide-tolerant:* • Wheat – none [1 ecological/environmental assessment] • Barley - none • Rice – none [3 ecological/environmental/geneflow assessment]
Modified starch in: • Potatoes • Maize	*Modified starch in:* • **Potatoes – 2 notifications** (Netherlands, 2004; Germany, 2004) • Maize – none
Modified fatty acid in: • Soybean • Oilseed rape	*Modified fatty acid in:* • Soybean - none • Oilseed rape – none [4 notifications (altered oil) for agronomic or production of materials/compounds]
Modified protein in: • Oilseed rape • Maize • Potatoes	*Modified protein in:* • Oilseed rape – none • Maize – none • Potatoes - none
High erucic acid in: • Oilseed rape	*High erucic acid in:* • Oilseed rape – none

Products NOT PREDICTED but PRESENT in variety trials 2003-2007:	• **Oilseed rape - 1 notification -** herbicide tolerant (glufosinate ammonium, incl. pollination control) – (UK, 2003)[a] • **Soybean – 1 notification** - herbicide tolerant (glyphosate)(Romania, 2007) • **Maize – 71 notifications** for herbicide tolerant, insect resistant and combined stacked events.

[a] Note: this release (B/GB/03/R38/1) was authorised but did not go ahead.

Based on notifications submitted under 2001/18/EC the majority of the Lheureux *et al*. predictions for medium term GM products do not appear to have been realised, or at least have not yet been realised. Fungi-resistant crops (wheat and fruit trees) have featured in Part B notifications, but so far all have been for agronomic, efficacy or environmental assessment trials, rather than for variety registration purposes. No notifications have been received for fungi-resistant oilseed rape or sunflower under 2001/18/EC. Similarly, there have been notifications for virus-resistant sugar beet, but again only for agronomic/efficacy trials, and there have been no notifications for virus-resistant potato, tomato, melon or fruit trees. Notifications have been lodged for herbicide-tolerant wheat and rice, but only for ecological/environmental assessment, indicating that these crop/traits still have some way to go along the testing route before seeking commercialisation.

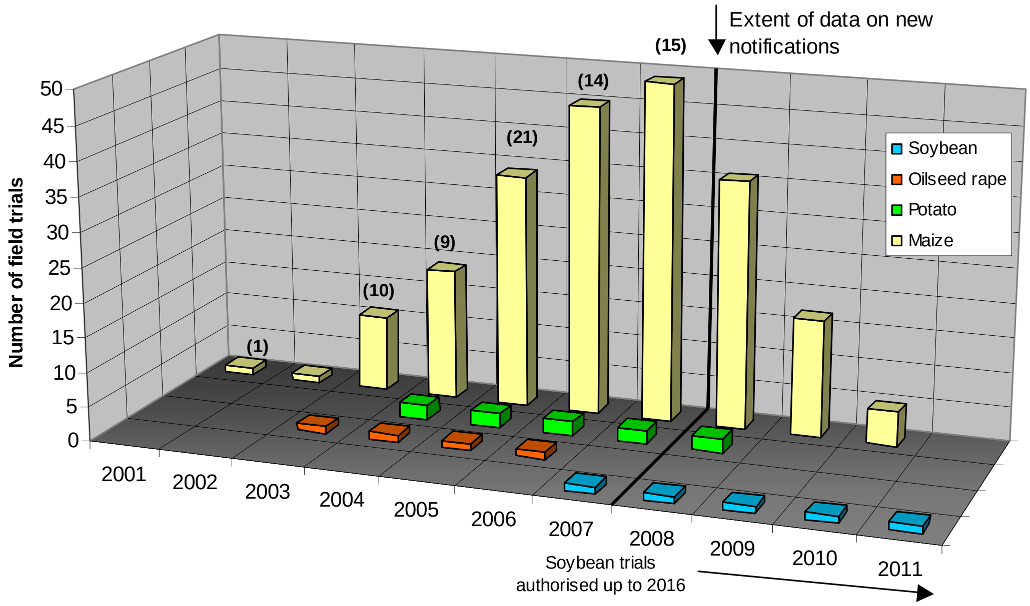
Similarly, predictions of modified fatty acids in soybeans and oilseed rape have not been fulfilled, and the same is true for modified protein in oilseed rape, maize, and potatoes. There have been notifications for oilseed rape with altered oil (although not necessarily for modified fatty acid content), but again none of the notifications were for variety registration purposes.

Where the predictions of Lheureux *et al*. do appear to have been realised is in the case of modified starch potatoes, with one notification in the Netherlands and one in Germany, both for variety registration purposes. The notifications, submitted in 2004 by BASF Plant Science GmbH, are for potato event EH92-527-1. This event, developed by Amylogene HB, Sweden, is for enhanced amylopectin starch for industrial applications (with the pulp to be used as cattle feed). The application, C/SE/96/3501, is currently pending authorisation for commercialisation, including cultivation.

Crop/trait combinations that have appeared in variety registration notifications, but were not predicted by Lheureux *et al*., include herbicide tolerant oilseed rape (1 notification, UK, 2003, although the trial did not take place), herbicide tolerant soybean (1 notification, Romania, 2007) and maize (71 notifications for herbicide tolerant, insect resistant and combined stacked events) (figure 9). Lheureux *et al*. made the prediction that herbicide tolerant varieties of these crops (maize, oilseed rape and soya) would be commercialised in the period 2003 to 2007, so the fact that variety registration notifications have been submitted may simply indicate that the approvals process is somewhat slower than was expected, and again this may in part be due to the 1999 *de facto* moratorium.

Lheureux *et al*. correctly predicted that there would be a rise in the number of notifications with stacked traits, particularly with regard to maize and cotton, and this certainly appears to be true for maize.

Figure 9: Number of active notifications for the purpose of variety registration.



Notes: Bars show the numbers of notifications that are active (i.e. new and ongoing) in each year. Numbers in brackets (shown only for maize) indicate the number of notifications submitted for variety registration purposes in each year. So, for example, in 2004 there were 9 new notifications for maize, plus the continuing active notifications from 2001 (1 ongoing in 2004) and 2003 (9 ongoing in 2004), making 19 active maize notifications in total. The graph therefore shows not only notifications, but also the timescales over which the consents operate, thereby giving the overall cumulative effect. Summary notification information is only available up to 2007, hence the upward trend for maize may continue beyond 2007 as additional notifications are submitted. [The single notification for soybean (in 2007) permits trials to continue until 2016, although the year axis has been curtailed at 2011 for clarity].

1.9 'Long term' pipeline GM products: predictions for 2008 - 2012

Based on information relating to GMOs under research and development in the laboratory, Lheureux *et al*. predicted the long-term pipeline list of GM products shown in column one of table 7. These crop/trait combinations are forecast for commercial release in the period 2012 and beyond. Given the expected 5-6 year period of field trials research before a GMO is likely to be ready for authorisation (Lheureux *et al*.), these crops and traits would be expected to be present as novel Part B field releases during the period 2003 to 2007. 'Novel' refers to crops/traits that are new in terms of EU DR notifications (although they may have been released elsewhere in the world), having only featured in Part B releases for a few years, and have not yet entered into the variety registration phase of development. Column 2 of table 7 shows the crops/traits as novel Part B notifications (bold) under 2001/18.

Up to the end of 2007 there had been eight notifications (equating to slightly less than 2% of all notifications) for GM plants resistant to abiotic stress factors (mainly drought, but also salinity). The crops involved were either maize or rice, and all notifications were for the purpose of agronomic or efficacy assessment. In addition there was a single notification for linseed (flax) with the enhanced ability to accumulate heavy metals (although, strictly speaking, this is not necessarily abiotic stress tolerance).

Lheureux *et al*. predicted enhanced yield as a future trait, although the report was not specific about the types of crops involved. The JRC data shows there have been 29 novel notifications for plants with enhanced yield over the relevant period, accounting for almost 7% of notifications. The species involved were maize, potato, rice and oilseed rape.

There have been a number of novel notifications submitted under 2001/18/EC involving the use of GM plants for molecular farming. This practice (also known as ‘pharming’) refers to the production of health-related or pharmaceutical compounds by GM organisms, including antibody production, pharmaceutical proteins and (edible) vaccines (but not including the production of enzymes for industrial processes). Species utilized are maize (3 notifications) and potato (1 notification), both of which were forecast by Lheureux *et al*., as well as oilseed rape and pea (1 notification each), which were not predicted. In their 2003 report, Lheureux *et al*. noted that pharming notifications were almost absent from EU field trials, which was at variance with GMOs in the laboratory R&D phase (11 % of projects involved traits with health-related compounds). The authors concluded that in Europe R&D activities in this field were limited to the early phase of development of GMOs and often to model “factory” plants (such as tobacco). The fact that field trial notifications are being submitted for such plants may indicate a shift from the development phase to a general field assessment phase, although it is still likely to be a number of years before commercialisation is sought.

For the year 2013 and beyond, Lheureux predicted the commercialisation of GM rice and vegetable plants with an enhanced content of “functional” food ingredients (such as vitamins and antioxidants, but also including hypoallergenic foods). Analysis of Part B notifications shows that, in line with their predictions, there has been some experimental activity of this type in the area of vegetables (i.e. potato and tomato), but there have been no notifications for rice. Interestingly, some of Lheureux’s predictions may seem to have been based on The Science and Technology Foresight Centre (Japan), which proposed a list of pipeline GM plants to be commercialised between 2011-2019 in Japan. Given that rice is a part of the staple diet in Japan, (much more so than in the EU) it might be expected to feature strongly in Japan’s list of potential GM pipeline products, and this perhaps illustrates the pitfalls of superimposing the tendencies of one country or area (Japan/SE Asia) on another (the EU). Plants with functional ingredients that were not predicted by Lheureux but which have appeared in Part B notifications are linseed (flax) with increased antioxidant capacity in seeds, maize with increased essential amino acid content in the grain.

Between 2003 and 2007 there were 2 novel notifications for GM trees with modified lignin content, both involving poplar, which shows some consistency with what was predicted. Conversely there have been no notifications under 2001/18/EC for GM hypoallergenic crops. Other novel part B trials have involved ‘functional’ crops, such as poplar genetically modified for the remediation of soils and *Arabidopsis thaliana* which changes of colour in the vicinity of explosives, for the detection of mines.

Table 7: Comparison of predicted and actual 'pipeline products' for beyond 2012. Years shown in brackets indicate the overall period of release of the trials(s)

Commercialisation predicted beyond 2012	**Actual** (novel Part B GMO trials 2003 – 2007)
GM plants resistant against abiotic stress factors (cold, salinity, drought)	• **Maize – 3 notifications** (drought tolerant, France, 2005-2010); • **Maize – 2 notifications** (drought (and herbicide) tolerant, France, 2003-2008); • **Rice – 3 notifications** (salinity and drought tolerant, Spain, 2003). • **Crops/traits not predicted:** • **Linseed/flax – 1 notification** (enhanced accumulation of heavy metals, Czech Republic, 2007-16)
GM plants with enhanced yield (all crops)	• **Maize – 1 notification** (France, 2005-2008); • **Potato – 9 notifications**: ▪ (Germany: 4, 2004-2011); ▪ (Netherlands: 1, 2004-2013); ▪ (Spain: 4 2005-2007); • **Rice – 15 notifications** (Spain, 2003-2003); • **Oilseed rape – 4 notification** (Sweden, 2006-2010);
GM plants for molecular farming (tobacco, maize, potato, tomato)	• **Maize – 3 notifications** (France: 2 notifications for gastric lipase for medical uses; 1 notification for expressing monoclonal antibodies for medical uses in cancerology; 2005-2008); • **Potato – 1 notification** (Germany: pharmaceutical and technical traits, 2006-2008) • **Crops/traits not predicted:** • **Oilseed rape - 1 notification** (Germany: synthesis of health-improving compound resveratrol and/or to reduction the phenylic compound sinapine, 2007-2008). • **Pea – 1 notification** (Germany: antibody production, 2007);
GM plants with an enhanced content of "functional" ingredients (rice, vegetables)	• **Potato – 1 notification** (Poland: higher antioxidant capacity, 2006-2010); • **Tomato – 1 notification** (Italy: accumulation of beta-carotene instead of lycopene, 2004). • **Crops/traits not predicted:** • **Linseed/flax – 1 notification** (Poland: increased antioxidant capacity of flaxseeds, 2006-10); • **Maize – 2 notifications** (France: increased essential amino acid content in the grain, 2003-2006).
GM trees with modified lignin content	• **Poplar – 2 notifications** (France: altered lignin content, 2003-12).
GM hypoallergenic crops	• None
Products NOT PREDICTED but PRESENT as novel Part B trials 2003-2007:	• **Poplar - 1 notification** – bioremediation of soils (Germany, 2003) • **Arabidopsis thaliana – 2 notifications** - change of colour in vicinity of explosives (Denmark, 2006 & 2007) • **Wheat – 1 notification** - enhanced protein content (Germany, 2006-8) • **Pea – 1 notification** - enhanced protein content (Germany, 2005-6) • **Birch – 1 notification** (Finland: flowering prevention, 2005-8) • **Linseed/flax – 1 notification** (Poland: improved properties of flax fibres & increased antioxidant capacity of flaxseeds, 2006-10) • **Potato – 2 notifications** (Germany: production of recombinant spider silk, 2003-5)

2. DEVELOPMENTS OUTSIDE OF EUROPE AND POTENTIAL CANDIDATES FOR GMO FIELD TRIALS IN EUROPE UP TO 2018

2.1 Introduction

As information on GMO under research under contained use is not readily available, reviewers of the development of GMOs have adopted a variety of approaches to predict what GMOs are likely to be developed for commercialisation. Standard approaches have been to survey companies and laboratories undergoing GM contained use research (Lheureux *et al*., 2003) or undertake structured consultations with scientists in the public sector and industry (Glover et al 2005) or extract information from a variety of online databases of field trials on a global scale (Dunwell and Ford 2005). For the purposes of this study, a review of GM crops that are being trialled in the USA and Canada, and a survey of the leading multinational agrochemical companies, were used as a barometer for the type of products that are likely to be presented for assessment in European GMO field trials in the long term.

The databases of GMO field releases in the US (APHIS, 2007d) and Canada (CFIA, 2007) between 2002 and 2007 were reviewed. Searches of these databases concentrated on the top 20 European crops[16], based on the area under production (table 8). As soybean, tomato and tobacco ranked in 2005 within the top ten of global applications for entry into GMO field trials (Dunwell and Ford, 2005), these species were also added to the search list. This approach, however, will exclude biotechnological developments in forestry, the majority of orchard crops, ornamental and grasses.

Table 8: European field crops and the development of GM varieties by 2005

Ranked area of EU production	Crop	GM varieties in field trials	Number of global GMO field trial applications by 2005	Ranking of no of global GMO applications by 2005[1]
1	Wheat	+	451	7
2	Barley	+	73	17 =[2]
3	Grain maize	+	6106	1
4	Forage maize	+		
5	Oilseed rape	+	1217	3
6	Durum wheat	+	3	50 =
7	Sunflower	+	52	22
8	Oats	+	2	51 =
9	Rye		No GMO trials	
10	Triticale		No GMO trials	
11	Potato	+	1223	2
12	Sugar beet	+	177	11

[16] Wheat, barley, grain maize, forage maize, oilseed rape, durum wheat, sunflower, oats, rye, triticale, potatoes, sugar beet, grapes, alfalfa/Lucerne, olives, field peas, clover, apples, cotton, rice.

13	Grape	+	60	20
14	Alfalfa/lucerne	+	417	8
15	Olive	+	2	51 =
16	Field pea	+	56	21
17	Clover	+	4	49 =
18	Apple	+	48	23
19	Cotton	+	962	5
20	Rice	+	323	10

After Dunwell and Ford (2005)

[1] Other top ranking GMO applications were soybean (4), tomato (6), tobacco (9)

[2] = More than one crop has the same ranking

The research that is coming forward from five leading companies (Monsanto, Pioneer Hi-Bred International Inc., Syngenta, Bayer CropScience and BASF) was examined using published website information.

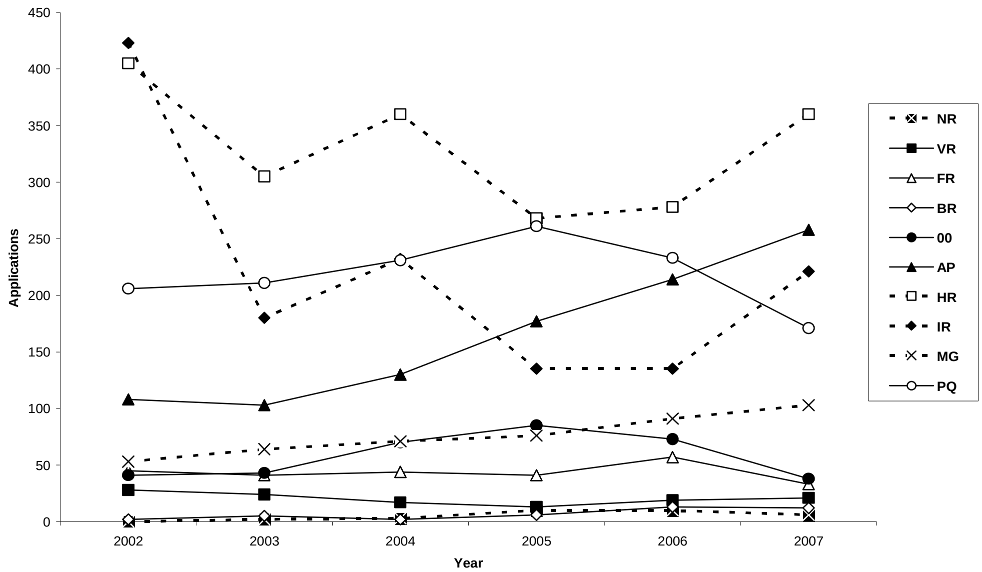
2.2 Analysis of applications of GMO field trials in North America

As already mentioned, during the last six years, there has been substantially more activity in the field testing of GM crop plants in the USA (> 6,800) and in Canada (>1,400) compared to the EU (>420).

- ***USA***

In the USA, almost 70% of the GMO field trials were carried out with maize, soybean and cotton. Compared with earlier analyses (Lheureux *et al.* 2003), there have been noticeable changes in the distribution of traits that have come forward in GMO field trials. Whilst the development of herbicide tolerant tolerance (29%) remained high, insect resistance was less prominent (19%) than it had been prior to 2002. Development of resistance to plant diseases (bacterial, fungal and viral) remained low (7%), as were categories like marker genes (7%).

Figure 10. Traits in GMO field trials in the USA between 2002 and 2007



Traits: NR – nematode resistance, VR – viral resistance, FR –fungal resistance, BR – bacterial resistance, OO – other, AP – agronomic properties, HR – herbicide resistance, IR – insect resistance, MG – marker gene, PQ - product quality.

The most noticeable features were that product quality (PQ) traits, which relate to food and feed use, accounted for 19% of the traits, which was as high as insect tolerance. The high-ranking traits within the PQ category were altered amino acid, protein and oil composition. There was also a progressive increase in agronomic properties (14%) (figure 10), of which drought resistance and yield increase featured highly.

A more detailed analysis of crop/trait combinations provides a clearer picture of what is emerging from the USA (table 9).

Table 9: Distribution of trait categories in USA GMO field trials between 2002 and 2007

Species	**00**	**AP**	**BR**	**FR**	**HR**	**IR**	**MG**	**NR**	**PQ**	**VR**	**Field trials approved**	**EU 25**
Maize	4%	14%	0%	1%	25%	31%	6%	0%	19%	0%	3427	*3/4*
Soybean	2%	13%	0%	5%	34%	7%	0%	3%	34%	1%	849	*22*
Cotton	1%	11%	0%	1%	49%	34%	1%	0%	2%	0%	409	*19*
Alfalfa/Lucerne	1%	0%	0%	0%	94%	0%	0%	0%	5%	0%	271	*14*
Wheat	4%	14%	0%	29%	34%	0%	2%	0%	18%	1%	196	*1*
Tobacco	14%	2%	1%	5%	5%	1%	7%	0%	59%	6%	125	*35*
Rice	18%	39%	6%	5%	21%	2%	4%	0%	6%	0%	124	*20*
Potatoes	2%	1%	0%	16%	0%	28%	8%	0%	25%	20%	100	*11*
Tomato	4%	2%	5%	7%	4%	5%	0%	0%	59%	15%	85	*23*
Barley	9%	0%	0%	36%	14%	0%	18%	0%	23%	0%	56	*2*
Sugar beet	0%	0%	0%	0%	75%	0%	0%	0%	0%	25%	28	*12*
Grapes	0%	0%	48%	43%	0%	0%	5%	0%	0%	5%	21	*13*
Apples	0%	0%	0%	0%	0%	6%	0%	0%	94%	0%	16	*18*
Oilseed rape	0%	25%	0%	0%	25%	25%	25%	0%	0%	0%	8	*5*
Sunflowers	0%	0%	0%	50%	0%	50%	0%	0%	0%	0%	4	*7*
Field peas	25%	0%	0%	0%	0%	0%	0%	0%	0%	75%	4	*16*
Triticale	0%	0%	0%	0%	0%	0%	0%	0%	100%	0%	1	*10*
No of traits	238	732	30	204	1723	1285	245	27	1189	65	5738	

Traits: AP – agronomic properties; BR – bacterial resistance; FR –fungal resistance; HR – herbicide resistance; IR – insect resistance; MG – marker gene; NR – nematode resistance; PQ - product quality; VR – viral resistance; OO – other

EU25 is a ranking of European crops based on area under cultivation (excluding aggregates of species) as used by Dunwell and Ford 2005.

Maize

Maize continues to be by far the most important crop in US GM field trials. Insect resistance (31%) followed by herbicide tolerance (25%), product quality or modified ingredients (19%) and agricultural properties (14%) were the dominant trait categories. Insect resistance continues to have a higher relevance than herbicide tolerance. Within the modified ingredients, altered compositions of proteins, starch and oils were the major traits accounting for 81% of the category. For agricultural properties, drought tolerance and yield increase were the major traits (65%).

Soyabean

Soybean is the major oil crop of the USA. Herbicide tolerance (34%) and product quality (34%) and agricultural properties (13%) are the major traits that have been present in trials for the last six years. Insect resistance (7%) were less prominent. Product quality traits consisted of changes to protein content and oil composition. For agronomic properties traits, yield increase was the predominant trait (55%). A small number of approvals included altered stem attributes (5%) and reductions in abiotic stress (5%).

Cotton

There have been few major changes in cotton since 2001; field trials have concentrated on herbicide tolerance (49%) and insect tolerance (34%). Reduced abiotic stress, particularly drought tolerance, accounted for approximately half of the approvals for agronomic properties (11%).

Alfalfa

Varieties with glyphosate tolerance that were released by Monsanto and one of their partners, Forage Genetics International, accounted for 94% of the GMO field trials in alfalfa. Forage Genetics International has also conducted field releases with alfalfa for altered lignin biosynthesis (5%).

Tobacco

Tobacco has been widely used as a model system for testing ‘proof of concept’ during transgenic trait development and had a broad distribution of traits. GMO field trials have focussed on product quality traits (59%). Where information has not been withheld on the grounds of confidentiality, the major trait in this category has been for reduced nicotine content. Tobacco is also a common platform crop for the production of plant-based pharmaceutical products as it is a leafy crop and can be harvested before flowering (Dunwell and Ford, 2005). Fourteen percent of the field releases were for the production of pharmaceutical proteins during 2002 and 2007. Other traits that have been introduced were improved fungal (5%) and viral (6%) resistance. Releases also took place for herbicide (glufosinate ammonium) tolerance (5%).

Rice

Rice is becoming an increasingly important global transgenic crop. It has been temporarily released in Iran and after extensive trialling in China it is awaiting regulatory approval (ISAAA, 2007). The Chinese focus has primarily been on producing higher yields and developing insect resistance. Although they have had transgenic varieties that have been in field trials since 1998 that are tolerant to either lepidopteran pests, bacterial blight, rice blast fungus, drought or salt tolerance (Katuria et al, 2007). In the USA field trials have concentrated on agricultural properties (39%), particularly increasing yield and the developing herbicide resistance (21%). In APHIS's category 'other properties', the predominant trait was enhanced proteins for human consumption (18%).

Cereals: wheat and barley

With the deferral of Monsanto's RoundUp Ready wheat programme in 2004, universities and trait development/gene discovery companies have largely undertaken breeding development in wheat (see BASF). Whilst the dominant trait was herbicide (glyphosate) resistance (34%), applications for this trait stopped after 2004. Field trials have concentrated on developing fungal resistance (29%), in particular resistance to *Fusarium* sp., and agricultural properties (14%), of which traits that increased yield were important. For quality traits (18%), alteration to protein and starch content were the dominant traits.

A similar situation is seen for barley, where American universities have carried out recent breeding activity. The main focus of activity has been in fungal resistance (36%), where developing traits for resistance to *Fusarium* sp., *Rhizoctonia* sp. and stem rust has been important. Transgenic varieties have also been bred for improving protein content and malting quality through the introduction of heat stable glucanase (product quality traits, 23%). For herbicide resistance (14%), GMO field trials have concentrated on the evaluation of phosphinothricin (glufosinate ammonium) tolerance.

Potato

Globally, potato is the second highest-ranking crop for GMO applications (Dunwell and Ford, 2005). In the USA as for wheat and barley, university and public funded organisations have made the majority of applications in the last six years. The dominant trait was insect resistance (28%), in particular the use of *Cry* proteins for controlling lepidopteran and coleopteran pests. Traits that control fungal diseases (16%), particularly late potato blight, and viral diseases (20%) were also prominent. For product quality traits (25%), the emphasis has been on reducing steroidal glycoalkaloids, altering protein, carbohydrate and vitamin E content and improving processing characteristics.

Tomato

Nearly sixty percent of GMO field releases for tomato have focussed on the quality of the fruit. The main traits have been increasing fruit quality, solid content, pigment composition, nutritional content, flavour and changing the sugar profile. The majority of the remaining traits have concentrated on improving viral (15%), fungal (7%) and bacterial resistance.

Sugar beet

Herbicide tolerance, in particular tolerance to glyphosate, remains the dominant trait (75%) for this crop. Some attention has also been given to improving viral resistance. The major notifiers in this crop have been Monsanto, Betaseed (a subsidiary of the European company KWS SAAT AG) and Syngenta.

Grape

The principal traits have been to improve bacterial (48%), fungal (43%) and viral (5%) resistance.

Apple

GMO field trials have been used to evaluate apple traits for improving apple product quality (94%) principally by reducing polyphenol oxidase activity.

Oilseed rape

There has been a reduction in the amount of field testing of oilseed rape relative to pre-2002. In contrast to Canada, a very small number of applications (8) have been come forward for field testing in the USA during 2002 and 2007.

- **Canada**

Caution must be exercised when reviewing novel trial data for Canada, as not all the modifications will have used recombinant DNA technologies (table 10). In contrast to the USA, oilseed rape is the predominant crop in Canadian confined field trials. This is followed by wheat, maize and soybean. A range of breeding activities can be seen in oilseed rape. The predominant trait was herbicide tolerance (34%), followed by male sterility/restoration (23%), which is a reflection of current hybrid production practice. Other traits include stress tolerance (17%), fungal resistance (11%) and oil modification. In comparison with US breeding programmes, a number of additional traits have been developed by Canadian universities, namely stress tolerance in alfalfa and potato.

Table 10: Distribution of trait categories in Canadian confined field trials between 2002 and 2007. Note that not all of these applications will be GM.

Species	PH	GR	MS/R	ST	FR	HR	IR	NC	MOC	VR	Total	EU 25
Oilseed rape	0%	1%	23%	17%	11%	34%	3%	4%	7%	0%	**601**	**5**
Wheat	0%	0%	0%	0%	13%	84%	0%	0%	0%	3%	**192**	**1**
Maize	0%	0%	0%	7%	3%	51%	36%	3%	0%	0%	**180**	**3/4**
Soybean	7%	3%	0%	0%	0%	78%	0%	7%	6%	0%	**72**	**22**
Alfalfa/Lucerne	0%	44%	0%	42%	0%	14%	0%	0%	0%	0%	**66**	**14**
Potatoes	0%	0%	0%	95%	5%	0%	0%	0%	0%	0%	**22**	**11**
Sugar beet	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%	**18**	**12**
Tobacco	82%	0%	0%	18%	0%	0%	0%	0%	0%	0%	**11**	**35**
Sunflowers	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%	**6**	**7**
Durum wheat	0%	0%	0%	0%	0%	100%	0%	0%	0%	0%	**5**	**6**
Barley	0%	0%	0%	0%	100%	0%	0%	0%	0%	0%	**1**	**2**
Tomato	0%	0%	0%	0%	0%	0%	0%	0%	0%	100%	**1**	**23**
No. of traits	**14**	**35**	**138**	**168**	**98**	**551**	**81**	**36**	**47**	**7**	**1175**	

Traits: PH – pharmaceutical product; GR – genetic research; MS/R male sterility/ restoration; ST – stress tolerance; FR –fungal resistance; HR – herbicide resistance; NC - Nutritional Change; MOC - Modified Oil Composition; VR – viral resistance.

EU25 is a ranking of European crops based on area under cultivation (excluding aggregates of species) as used by Dunwell and Ford 2005.

- **Stacking**

A hurdle in the transition from first generation ‘input’ traits to the second generation ‘output’ traits has been the ability to develop technologies for the co-ordinated manipulation of multiple genes or traits (Halpin, 2005). Whilst hurdles still exist for extensive alteration of plant metabolic pathways, new techniques have been introduced that have enabled more genes to be inserted into plants (‘stacking’). Compared with stacking levels six years ago, there have been noticeable increases in the number of genes that have been inserted into GMOs particularly in maize, soybean and cotton (table 11). More stacked genes are being seen in commercial material as a result and from the evidence accumulated from the multi-national company’s pipelines we can expect stacking to become a common feature of many more transgenic agricultural crops in the future.

Table 11. Comparison of stacked genes in US field trials for selected crops between 1991 and 2002 (91-02) and 2002 and 2007 (02-07) (% of approvals)

Plant/ No. of traits	GMO field trials containing stacked genes in US field trials (% of approvals for each crop)									
	Maize		Soybean		Cotton		Wheat		Tobacco	
	91-02	02-07	91-02	02-07	91-02	02-07	91-02	02-07	91-02	02-07
1 trait	85.0	55.3	96.3	57.2	91.8	70.9	98.8	91.3	98.1	93.4
2 traits	14.8	28.4	3.7	27.0	8.2	25.9	1.2	5.1	1.9	5.9
3 traits	0.2	10	0	4.3	0	3.2	0.0	0.5	0	0.7
> 3 traits	-	6.3	-	11.5	-	0	-	3.1	-	0.0
Number of approvals	4,018	3427	644	849	587	409	256	196	212	125

Data for 1991 to 2002 was taken from Lheureux *et al.* (2003)

2.3 Production of plant-made pharmaceutical products

The number of permits for plant-made pharmaceutical products that have been issued for the last four years have declined to an average of 11 permits per year, compared with 28 permits between 1999 and 2002. Expectations, however, are that this sector will expand globally by 100% in the forthcoming five years (Dunwell and Ford, 2005). Despite the predicted expansion in this area, there are currently no plans in the USA to deregulate any crops expressing these products and they will continue to be grown under permit licence conditions.

A variety of food and industrial crops have been approved for use for the production of these products including maize, barley, rice, pea and tobacco and safflower in the last four years. These crops have been grown under strict permit conditions, where large isolation distances, constant monitoring including high levels of inspection and safe disposal of waste material after harvest have been applied. APHIS has required long isolation distances for these crops, e.g. 6 km for maize, 0.4 km for rice including a fallow zone of 15m around the GM crop and 0.4 km for barley (which is 99% self-pollinating) with a fallow zone of 15 metres around the GM crop.

Dunwell *et al.* 2005 point out that as the plant itself is not the desired end product, production platforms can be more flexible and containment issues may be more easily addressed. For example, in tobacco if the product is expressed in the leaves, harvesting can take place before flowering for which there is established process. However, alternative non-crop species are being developed to prevent contamination of conventional food and feed crops which includes the use of algae, moss, duckweed or the use of greenhouse crops that do not require flowering (lettuce, alfalfa and potato).

A number of plant-derived products are already available in Europe that have been produced by crops in the US. These are mainly diagnostic and laboratory agents. A second wave of plant-derived products including a range of human vaccines and antibodies will become available (Dunwell and Ford 2005). To date, there are over 20 plant-derived pharmaceuticals that have been submitted for clinical trials, including recombinant antibodies, human and edible vaccines. Six plant-derived technical proteins are available (avidin, trypsin, ß-glucuronidase, aprotinin, lactoferrin and lysozyme) (Zika et al, 2007).

2.4 Pipeline products for the main companies in biotechnology based on annual reports, and company website information.

In the following section, company crop product names are described in the text, for information on the GM events and their characteristics refer to table 12 at the end of section 2.4.

- *Monsanto (2008)*

Currently the seed and genomics section of Monsanto principally markets glyphosate and other glyphosate-based herbicide tolerant traits for maize, soybean, cotton and oilseed rape and insect resistant traits, mainly in maize and cotton. They also market seed of a wide range of conventionally bred agricultural and vegetable crops.

In the past six years the company has upgraded its earlier commercialised herbicide and insect tolerance products, e.g. Bollgard I insect resistant cotton with Bollgard II and Roundup Ready Cotton with Roundup Ready Flex Cotton and has marketed stacked hybrids of these products, e.g. Bollgard II with Roundup Ready Flex. The level of stacked genes in maize also increased, with triple stacked varieties combining multiple insect resistance genes with herbicide tolerance.

This process of upgrading and the increased use of stacking is planned to continue over the next decade. Further upgrades in insect tolerance in Maize (Yield Gard VT PRO, Yield Gard Rootworm III) and Cotton (Bollgard III) are planned, as is herbicide tolerance in Soybean (Roundup Ready 2 Yield). In the same period insect resistant traits are planned for introduction in Soybean (Insect Protected Roundup Ready 2 Yield).

Through a network of subsidiary companies and collaborative partner agreements, Monsanto is accelerating and broadening its development programme. Examples are cross-licensing agreements with BASF in developing drought tolerant maize and with Dow Agrosciences in developing SmartStax maize, an eight gene stack, providing multiple combinations of insect and herbicide resistance (Dow AgroSciences 2007).

Additional agricultural traits that are being developed include grain yield in maize, soybean and oilseed rape; drought resistance in maize and cotton, nitrogen utilisation in maize; nematode resistance in soybean and disease resistance in soybean.

For products with output traits (value-added traits) the company is continuing to focus on producing crop varieties that improve processing and nutritional value in food, feed and fuel production through lipid, protein and carbohydrate enhancement. Examples are high lysine in maize; high oil content in soybean and maize; low linolenic acid and saturate content in soybean and Omega-3 enriched Soybean.

- *Pioneer Hi-Bred International Inc, Dupont (2007)*

Pioneer Hi-bred International, Inc, a Dupont business, markets a wide range of crops worldwide in alfalfa, maize, mustard, oilseed rape, pearl millet, rice, sorghum, soybean, sunflower and wheat. Prior to this merger, Pioneer and Dow AgroSciences collaborated in 1995 to develop insect resistant traits which led to the production of Herculex 1 maize in 2003, providing corn root worm resistance and glufosinate tolerance. Three years later glyphoshate tolerance and corn borer resistance were added to Herculex 1 to form the double stacks, Herculex RW and Herculex Xtra respectively. Triple stacks have also been commercialised by adding Roundup Ready 2 with Herculex RW and Herculex Extra.

Before 2003 Hi-bred International and Dupont had USA approved commercial GM herbicide tolerance, insect resistance and male-sterility in maize, herbicide tolerance in cotton and altered fatty acids and oils in soybean. Over the last six years, they extended their established market platform in corn root worm resistance in maize. The company is seeking regulatory approval in the USA for a multiple insect resistant (corn borer and rootworm) and dual herbicide (glufosinate and glyphosate) tolerant stack, through their Optimum AcreMax products.

For agricultural traits, Pioneer Hi-Bred International plans to upgrade their insect resistance traits in maize and introduce the trait into soybean and rice. For herbicide tolerance they are combining glyphosate and acetolactase (ALS) tolerant traits for maize, soybean and cotton. Triple stack herbicide tolerance is also at the early development stage for maize and proof of concept stage for soybean. Glyphosate tolerance is planned for introduction in oilseed rape and alfalfa, and insect resistance for rice. Additional agricultural pipeline traits include grain yield in maize and soya, drought tolerance and nitrogen use efficiency in maize, fungal resistance in maize and soybean and cyst nematode resistance in soybean.

For value-added traits Pioneer Hi-Bred International is concentrating on improving increased ethanol production through higher levels of fermentable starch and simple sugars in maize. Improved feed traits are planned for both maize and soya. The company is also continuing to work on the development of alternation of oil composition by producing soybean with high oleic and high stearic acids and low linoleic acids.

- *Syngenta (2007)*

Syngenta was formed as part of a merger of two major crop biotechnology businesses Novartis and Astra Zeneca. It is a leading agrochemical company with an expanding seeds sector, which in 2007, accounted for 28% of its sales. Seeds for field crops include corn, soybean, other oilseeds and sugar beet and vegetable and flower seeds. The company is engaged in the development of enzymes and traits which have the potential to enhance agronomic, nutritional and biofuel properties of plants.

Moving from their early insect and herbicide tolerant maize (Bt 11) products, the company has developed a series of herbicide and insect resistance traits under the brand product Agrisure, which are stacked combinations of either events GA21 or MIR604. Their triple stack maize Agrisure 3000GT is now available (2008) for commercial sale in the US. Syngenta anticipates that its triple stack series in maize will have reached 60% of its maize portfolio by 2018. The company has plans to continue to upgrade and introduce further insect resistant and herbicide tolerant traits in maize and soybean.

For agricultural traits, improved nitrogen efficiency is being developed in maize. Whilst for output traits the company is developing maize with enhanced levels of amylase for biofuel production and elevated levels of phytase for animal feed.

- *Bayer CropScience. (2006)*

Bayer CropScience was created in 2002 as a subsidiary of the German company Bayer AG, following the merger of Bayer's Crop Protection Group and Aventis CropScience. Bayer CropScience has three sectors to its business: agrochemicals, chemicals for use in land management and seeds. The company currently markets four crops: vegetables, rice, cotton and oilseed rape, of which insect resistant/herbicide tolerant oilseed rape and cotton have a prominent share of the North American market.

Aventis CropScience had US market approval for a wide range of herbicide tolerant traits under their brand name LibertyLink (glufosinate ammonium) in maize, oilseed rape, soya and rice. They also used this trait to develop a system for producing hybrid varieties (Seed Link) of consistent quality with high yields. The system can also be characterised for the production of insect resistance varieties. Bayer CropScience has made agreements with Dupont and Pioneer for the inclusion of

Bayer CropScience's traits, particularly those for glufosinate ammonium tolerance, into Pioneer's maize development seed programme.

Their research pipeline will include polyunsaturated fatty acids and specialised oils in oilseed rape, developing the next generation of agronomic and quality (output) traits in cotton and expansion of rice hybrid varieties (Scheitza, 2006).

- *BASF (2008)*

BASF is a chemical company that specialises in a broad range of products in the chemical, plastic, oil and gas and agricultural sectors. In the agricultural sector it is a supplier of seed, produce and chemicals to the farming, food processing, pharmaceuticals, animal and human nutrition industries.

The company has had an established platform of imidazolinone herbicide tolerant (non-GM) varieties in sunflower, rice, wheat and maize. With transgenic material, the company has US market approval for food and feed use of oilseed rape with elevated levels of the enzyme phytase, which assists animal nutrition by making more phosphorous available from plant sources. The company is awaiting EU approval for cultivation and industrial use of the starch potato (EH92-527-1) and has developed a potato that has resistance to the fungal disease potato late blight (*Phytophthora infestans*), which is undergoing GM field trials in Europe. Their research and development programme has three components: 1) agricultural traits, i.e. high yields, drought tolerance, nematode resistance and fungal resistance, 2) product quality traits, i.e. improved amino acid content, poly unsaturated fatty acids and carotenoid content and 3) renewable raw materials, i.e. amylopection in potato.

To expand and intensify their research programme BASF has entered into collaboration with Monsanto. This will enable both companies to exchange material and provide a series of updates and products within crop groups. The programme is focusing on maize, soybean, cotton and oilseed rape. The joint programme will concentrate on drought tolerance, higher yields and nitrogen utilisation in maize and higher yields in soybean (Marcinowski, 2008).

BASF are also cooperating with the Australian Molecular Plant Breeding Cooperative Research Centre (MPBCRC) to develop high yielding wheat varieties that are at the same time more resistant to fungal diseases and adverse environmental conditions such as drought.

Table 12: Company Product Names

Species	Product Name	GM Event	Characteristic
	Yield Gard VT Rootworm	MON 88017	Resistance to corn rootworm
Cotton	Bollgard I	Mon 531	Lepidopteran resistant; Cry1Ac; from *Bacillus thuringiensis* (Bt)
Cotton	Bollgard II	Mon 15985	Lepidopteran resistant; Cry1Ac and Cry2Ab2 from *Bacillus thuringiensis*

			(Bt)
Cotton	Roundup Ready Cotton	Mon 1445	Glyphosate tolerant; 5-Enolpyruvylshikimate-3-phosphate synthase (EPSPS); from *Agrobacterium* sp. strain CP4
Cotton	Roundup Ready Flex Cotton	Mon 88913	Glyphosate tolerant; 5-Enolpyruvylshikimate-3-phosphate synthase (EPSPS); from *Agrobacterium* sp. strain CP4
Maize	Agrisure 3000GT	MIR604+Bt11+GA21	See individual traits
Maize	Agrisure CB/LL	Bt 11	European Corn Borer resistant; Cry1Ab; from *Bacillus thuringiensis* (Bt)
Maize	Agrisure CB/LL/RW	MIR604+Bt11	See individual traits
Maize	Agrisure GT	GA21	Corn rootworm resistant; modified Cry3A from *Bacillus thuringiensis* (Bt)
Maize	Agrisure GT/CB/LL	Bt11+GA21	See individual traits
Maize	Agrisure GT/RW	GA21+MIR604	See individual traits
Maize	Agrisure RW	MIR604	Corn rootworm resistant; modified Cry3A from *Bacillus thuringiensis* (Bt)
Maize	Herculex 1	1507	Cry1F Western Bean Cutworm, Corn Borer, Black Cutworm and Fall Armyworm resistance Glufosinate herbicide tolerance
Maize	Herculex RW	59122-7	Cry34/35Ab1 Western Corn Rootworm Northern Corn Rootworm Mexican Corn Glufosinate herbicide tolerance
Maize	Herculex Xtra	1507 + 59122-7	See individual traits
Maize	LibertyLink	T25	Glufosinate tolerant; Phosphinothricin acetyl transferase (PAT); from Streptomyces viridochromogen
Maize	Roundup Ready 2	NK 603	Glyphosate tolerant; 5-Enolpyruvylshikimate-3-phosphate synthase (EPSPS) from *Agrobacterium* sp. Strain CP4
Maize	Smartstax	MON 88017 + NK603 + MON89034 + 1507 + 59122-7 + T25	See individual traits
Maize	Yield Gard	Mon 810	Lepidopteran resistant; Cry1Ab; from *Bacillus thuringiensis* (Bt)
Maize	Yield Guard VT PRO	MON89034	Cry 1A.105 +Cry 2Ab2, European corn borer, fall armyworm, black cutworm, and corn earworm
Potato	-	EH92-527-1	Altered starch composition (higher amylopectin:amylose ratio)

Soybean	Roundup Ready 2 Yield		Glyphosate tolerant; 5-Enolpyruvylshikimate-3-phosphate synthase (EPSPS); from *Agrobacterium* sp. strain CP4

GM Event Information on Maize: Yield Gard Rootworm III, Optimum AcreMax; Cotton: Bollgard III and Soybean: Insect Protected Roundup Ready 2 Yield are not known.
Sources:
National Corn Crowers Association – NCGA,
http://www.ncga.com/biotechnology/Search_hybrids/know_where.asp
USA database of of Completed Regulatory Agency Reviews
http://usbiotechreg.nbii.gov/database_pub.asp
EFSA GMO Application website:
http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_GMOApplications.htm

2.5 Summary and long-term prediction

Analysis of USA GMO field trials shows two lines of evidence to suggest they are experiencing a shift from first generation input traits (designed for simplified agronomic production) to second generation output traits, or product quality traits. These are designed to produce food and feed products with enhanced qualities. In the USA there is, therefore, increased use of traits with altered protein, carbohydrate and oil composition in maize and soybean in a particular. The other noticeable feature has been an increase in agricultural properties that will maintain higher yields under drought stress. These traits will be increasingly important for maize and cotton production where water is at a premium. Maize varieties with enhanced drought tolerance are very near commercialisation.

Since the withdrawal of Roundup Ready cereals (barley and wheat), public and university funding have provided most of the support for transgenic cereal research programmes. Whilst there is activity in developing fungal resistance in cereals, the withdrawal of agrochemical company support in these crops will inevitably slow down the short-term development of transgenic varieties in these crops. However, there is more interest from multinational companies in developing potato, particularly in reducing potato pests and diseases and its extended use into non-food applications (Mullins et al, 2007; Chakravartay, et al, 2007).

It would appear that the range of crops and wide use of traits has narrowed with time, which concurs with what has been witnessed in Europe. For the most part, the development of transgenic crops appears to have become aligned to the seed and variety programmes of the multi-national agrochemical companies. As a result the major activities have been restricted to maize, soybean, cotton, alfalfa, rice and oilseed rape.

Further narrowing in the short-term may also have resulted from companies concentrating their existing resources on improving their existing crop portfolios by producing crop varieties which provide the grower with a wider range of herbicide tolerant, insect resistant and product quality traits through gene-stacking. Companies are also collaborating and exchanging genetic material so that a broad range of traits can be placed in these multi-stacked varieties, which might also explain why the pipeline appears to have narrowed.

From the evidence we have gathered, a tentative long-term forecast for GMOs in the European pipeline to 2018 is given in table 13 below.

Table 13: Updated pipeline for GMOs entering in the European GMO field trials based on activity in USA and Canada

Period 2008- 2012	**Period 2013 to 2017**	**Period after 2018**
Product development (within next 5 years) **Agricultural Benefits** Upgrading and extended range of herbicide tolerant maize, soybean and cotton Upgrading and extended range of insect resistant maize and cotton Herbicide tolerance in alfalfa High oil maize[1] Drought resistant maize[1, 2] Insect-resistant traits in soybean[2] Fungal resistance in maize[3] **Food and feed** Modified fatty acid (high oleic[3], stearic, low linolenic) soybean[1, 2]	**Trait development (next 5 to 10 years)** **Agricultural Benefits** High yield maize[1, 2], soybean[2] and oilseed rape[2] Nitrogen utilization maize[2, 4] Drought resistant cotton[2] Nematode resistant soybean[2, 3, 4] Stress tolerant oilseed rape Insect resistant rice Fungal resistance in potato, wheat, barley and oilseed rape Virus resistant sugar beet Modified fatty acid (stearic) soybean[2, 3] Improved animal feed in maize[4] and soybean[3] Improved oils in oilseed rape	**Gene discovery (more than 10 years)** **Agricultural Benefits** Virus resistance in potato, tomato, tobacco
Renewable resources/biofuels Amylopectin in potato[1] Amylase and Lysine in maize (improved ethanol processing)[2, 4]	**Biopharming** GM plants for molecular pharming (tobacco, maize, barley, rice and safflower)	**Renewable resources** Forestry yield/processing [1]

Sources: [1]Kast (2007), [2]Casale (2008), [3]Pioneer (2008), [4]Syngenta (2007)

2.6 New approaches to the production of genetically modified plants

In parallel with the expansion of new GM crops and new GM traits there is also the ongoing development of new techniques for introducing desired characteristics into crop plants. These novel plant modification techniques are being developed to speed up the GMO production process, and to enhance the precision and specificity of the induction or selection of desired properties (e.g Vain, 2007, Schouten *et al*, 2006).

For a novel organism to definitely fall under the scope of the Directive it must have been developed using certain defined techniques. Types of genetic modification that are specifically mentioned in Council Decision 2002/813/EC[17] are: insertion of genetic material; deletion of genetic material; base substitution; and cell fusion. Methods used in the process of modification that are specifically mentioned are: transformation; electroporation; macroinjection; microinjection; microencapsulation and infection. However the Directive uses the wording '*inter alia*', and it is clear from both it and 2002/813/EC, that the types of genetic modification that fall under the legislation, and the methods used to achieve them, are not limited to the above techniques.

With the advancement of these techniques the distinction between genetic modification and other plant biotechnology methods is becoming increasingly narrow. As the technology advances there is the possibility that scientific developments may exceed the legislative frameworks that have been put in place to manage them. This raises the question as to whether new ways of introducing desirable plant characteristics might fall outside the scope of the Directive, resulting in the deliberate release of plants that, simply by default, are unregulated by the legislation.

It was beyond the scope of this study to review these techniques and their implications from a legislative perspective. Reviews have been undertaken to examine some of these issues, for example by the Belgian Advisory Council Secretariat (BBAC, 2007), the Netherlands' Commissie Genetische Modificatie (e.g. COGEM, 2006a, COGEM 2006b) and the UK's Advisory Committee on Releases to the Environment (ACRE, 2007). In order to bring clarity to these discussions and to harmonise the approach of Member States, the European Commission has recently established a Working Group to evaluate a list of new techniques for which it is unclear whether they result in genetic modification[18]. It is anticipated that the Working Group will report in 2009.

[17] COUNCIL DECISION of 3 October 2002 establishing, pursuant to Directive 2001/18/EC of the European Parliament and of the Council, the summary notification information format for notifications concerning the deliberate release into the environment of genetically modified organisms for purposes other than for placing on the market.

[18] Working group on the establishment of a list of techniques falling under the scope of Directive 2001/18/EC on the deliberate release of genetically modified organisms into the environment and directive 90/219/EEC on the contained use of genetically modified micro-organisms.

3. SUMMARY

1. From the analysis of Part B notifications under the Directive from 2001 to 2007 it emerges that a single crop, maize, now dominates, accounting for almost 58% of GMO field trials. Other prevalent crops in Part B trials are potatoes, at almost 15%, cotton at around 6% and oilseed rape at 3%. This situation is something of a shift from that reported by Lheureux *et al*. in 2003, when four main crops of maize (26%), oilseed rape (20%), sugar beet (16%) and potato (11%) dominated. In addition the number of plant species in Part B notifications has also decreased, and there appears to be a tendency to concentrate on the ‘major’ agricultural crops used for animal feed and for industrial use. This may be symptomatic of the reduction in the number of SMEs and research establishments putting forward notifications. It is also apparent that there is an increasing use of stacked events, including multiple herbicide tolerance and multiple insect resistance in these crops, providing better protection from insect pests, and allowing growers to simplify their crop management practices.

2. During the early years of GM plant development developers focussed mainly on agronomic input traits (herbicide tolerance, insect resistance, resistance to pathogens, etc.). These so-called “first generation” GMOs were mainly concerned with increasing productivity, simplifying crop management and reducing costs to growers. In 2003, when Lheureux *et al*. published their review, it was expected that there would be a move towards GMOs that would embrace new products and be targeted more towards consumer expectations. These so-called “second-” and “third generation” GM crops were expected to lead to improved food quality, deliver new medicines, contribute towards preventing disease/reduce health risks, and to improve interactions between the crop and the environment.

3. Lheureux’s predictions have been most accurate in the short-term (as might be expected), with the marketing of crops such as herbicide tolerant and insect resistant maize and cotton (both single and stacked events), herbicide tolerant oilseed rape, soya and sugar beet. However, assessment of the notifications submitted under 2001/18/EC (from 2001 to 2007) shows that, overall, GM crops and traits are five or more years behind what was predicted by Lheureux *et al*. in 2003. An example of this is modified starch potatoes (predicted to be commercialised in the date range 2003-2007, but now actually due to be commercialised in 2008). In many other cases, however, the developments predicted by Lheureux *et al*. appear to have come to a standstill, at least in terms of EU trials. Examples are herbicide tolerant wheat, virus-resistant sugar beet, modified fatty acid in soybeans and oilseed rape, plus many other crop/trait combinations, none of which have been present in variety registration trials between 2003 and 2007. All these crop/trait combinations appear in Lheureux’s ‘medium-term’ pipeline list. Surprisingly, the ‘long-term’ list appears to be more accurate, although the fact that certain crops/traits appear in novel Part B trials does not guarantee they will eventually be commercialised.

4. Looking to the USA and Canada, where GM technology has found greater acceptance than Europe, maize, soybean and cotton have been the major focus of GM field trial activity. Herbicide tolerance has been the single most utilised trait, but product quality traits have also accounted for the same number of trials as insect

tolerance. Product quality traits include, for example, altered amino acid, protein and oil composition. Agronomic properties such as drought resistance and yield increase also featured highly. There have also been noticeable increases in the number of genes that have been inserted, or stacked, into GMOs, in particular for maize, soybean and cotton. As a result more stacked genes are being seen in commercial material. The review of the multi-national company's pipelines suggests we can expect stacking to become a common feature of many more transgenic agricultural crops in the future, which will inevitably bring complications for detection and labelling in Europe.

5. Reviewing progress in Europe against predictions made by Lheureux *et al.* and the current situation in the USA, the EU is likely to see a continuation of notifications for crops with stacked events. In the long term there is likely to be a greater number of Part B applications for industrial crops producing novel compounds and fibres, etc., as well as crops producing health-related or pharmaceutical compounds. However, a recent desk study on technologies for biological containment of GM and non-GM crops concluded that field crops are unlikely to be the vehicle for any future specialised production of plant-made industrial products and pharmaceuticals, with non-food crop systems in contained facilities being the method of choice in the future[19]. GM species with special properties, such as soil bioremediation, and indicator species allowing the detection of noxious/harmful substances may also be present in part B trials, although the number of such notifications will probably remain at a relatively low level. It is also foreseeable that the number of notifications for crops with enhanced yield will continue to increase as more pressure is put on existing crop production due to the demand for food and biofuel.

6. In parallel with the expansion of new GM crops and new GM traits there is also the ongoing development of new techniques for introducing desired characteristics into crop plants. The European Commission has recently established a Working Group to examine whether plants developed by these techniques will be classified as GMOs. It is conceivable that a technique that is deemed to give rise to a GMO, and which therefore falls within the scope of the Directive, may not be taken forward for commercial development because of the costs, time and political uncertainty associated with gaining authorisation to release a GMO. However, the review of the programmes of the major plant breeding and biotechnology companies indicates that they have plans to keep developing plants based on GM technology for the foreseeable future.

[19] Research funded by UK Department for Environment, Food and Rural Affairs, see: http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&Completed=0&ProjectID=13020#Description

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