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# 2020 Outlook: The GM crops global pipeline and New Plant Breeding Techniques

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Joint Research Centre

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**Int. Workshop of GMO-analysis networking**

Varese

21-23 July 2015

# OUTLINE

- **The global pipeline of GM crops**
  - 2008 study
  - 2014 update: analysis of results
- **Future trends in Biotechnology**
- **New Plant Breeding Techniques**
  - State-of-the-art
- **Conclusions**

# The global pipeline of GM crops

# GM crop pipeline: 2008 Study

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- **JRC Report (available at http://ipts.jrc.ec.europa.eu/)**
- **Scientific publications**

JRC Scientific and Technical Reports

**The global pipeline of new GM crops**

**Implications of asynchronous approval for international trade**

Authors: Alexander J. Stein and Emilio Rodríguez-Cerezo

EUR 23846 EN - 2009

JRC EUROPEAN COMISSION

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## International trade and the global pipeline of new GM crops

**To the Editor:**

In a previous issue, Paul Christou and colleagues[1] highlighted the patchwork of laws and regulations governing tolerance levels for *approved* genetically modified (GM) material in non-GM food and in the labeling and traceability of GM products. A related but different problem is that of 'asynchronous approval' of *new* GM crops across international jurisdictions, which is of growing concern due to its potential impact on global trade. Different countries have different authorization procedures and, even if regulatory dossiers are submitted at the same time, approval is not given simultaneously (in some cases, delays can even amount to years). For instance, by mid-2009 over 40 transgenic events were approved or close to approval elsewhere but not yet approved—or not even submitted—in the European Union (EU; Brussels) (for more details, see **Supplementary Data**). Yet, like some other jurisdictions, the EU also operates a 'zero-tolerance' policy to even the smallest traces of nationally unapproved GM crops (so-called low-level presence). The resultant rejection of agricultural imports has already caused high economic losses and threatens to disrupt global agri-food supply chains[2–8].


To assess the likelihood of future incidents of low-level presence of unapproved GM material in crop shipments and to understand related impacts on global trade and the EU's agri-food sector, we compiled a global pipeline of new GM crops. Our motivation was to obtain a realistic estimate of how many new GM crops will be commercialized in the next years, by whom and in which countries—and when these new crops will be authorized by the different trading partners of the EU. In this context, we invited a select panel of national regulators, industry representatives, experts from national and international research institutes and actors from the global food and feed supply chain to a workshop organized at the Institute for Prospective Technological Studies of the European Commission's Joint Research Centre in November 2008 to discuss for the first time the issue of low-level presence in view of a growing global pipeline of new GM crops. (For more details, see **Supplementary Notes**.)

# GM crop pipeline: 2008 Study

**Context of the study**: first incidents of GM crop Low Level Presence (LLP) and consequent trade disruption.

**Main objective**: to assess the likelihood of future LLP incidents of unapproved GM material in crop shipments and to understand related impacts on global trade and the EU´s agri-food sector.

**Main results**:

- 42 GM events authorised in at least one country, of which 33 cultivated
- Main GM crops: Cotton, Maize, Soybean, Oilseed rape
- Main traits: Insect resistance, Herbicide tolerance
- Main developers: US- and Europe-based Multinational Companies
- Projections 2014:
  - 103 GM events on the market (higher LLP risk)
  - Half of new GM events brought to the market by players from developing countries
  - Quality traits slowly emerging

# GM crop pipeline: 2014 Study

**Objectives**: to depict the orientation taken by biotechnology innovations in agriculture and its consequences for many actors in the commodity supply chain and regulatory/authorization bodies.

**Methodology**: build a database of GM crops in the following development stages:

| | |
|---|---|
| **Marketed crops** | GM events that are currently cultivated and commercialized in at least one country worldwide |
| **Crops at Pre-commercial stage** | GM events that are authorized for cultivation in at least one country worldwide but not yet marketed |
| **Crops at Regulatory stage** | GM events that are under assessment for authorization in at least one country worldwide |
| **Crops at Advanced R&D stage** | GM events not yet in the regulatory process but at late stages of development. |
| **Crops at Early R&D stage** | GM events for which a proof of concept has been obtained. |

# GM crop pipeline: 2014 Study

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## Sources of information:

- Public databases of approved GM crops
- Databases of the national public authorities
- Information available online on the GM crops pipeline of private companies
- **International workshop (11-12 June 2014 at JRC-IPTS):**
  - National regulators from the EU, the US, Canada, Brazil, China, India, Turkey, Australia and Africa.
  - The Food and Agriculture Organization (FAO)
  - The main private technology providers of GMOs
  - Public Technology Providers and Public-Private Partnerships in the field of GM crops development
  - Stakeholders from the food/feed supply chain

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# Future trends in biotechnology

## Intellectual Property

**Expiry of patents** of broadly cultivated and exported GM crops:
- November 2014: MON810 maize
- March 2015: 40-3-2 soybean

## Technological developments

**RNA interference** is increasingly used to obtain a stable gene silencing effect in transgenic plants. The R&D is very active and some products are at an advanced stage.

**New Plant Breeding Techniques (NPBT)**

# New Plant Breeding Techniques

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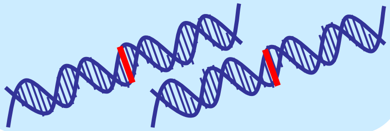
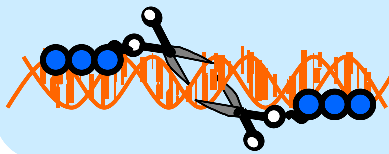
## TARGETED MUTAGENESIS TECHNIQUES

OLIGONUCLEOTIDE DIRECTED MUTAGENESIS



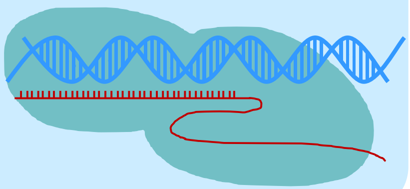
ZINC FINGER NUCLEASE TECHNIQUE



MEGANUCLEASE TECHNIQUE

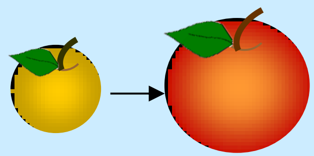
TALEN TECHNIQUE

CRISPR-Cas SYSTEM

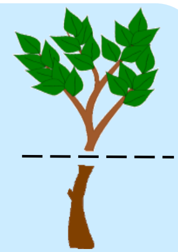


## VARIANTS OF PLANT TRANSFORMATION TECHNIQUES

CISGENESIS AND INTRAGENESIS

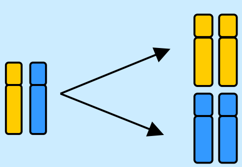


GRAFTING ON GM ROOTSTOCK

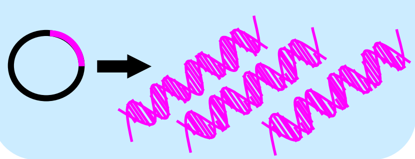


## TECHNIQUES RESULTING IN "NEGATIVE SEGREGANTS"

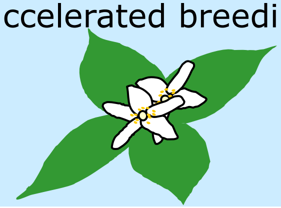
REVERSE BREEDING



RNA DIRECTED DNA METHYLATION



EARLY FLOWERING-accelerated breeding



# New Plant Breeding Techniques

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- **JRC Reports**
- **Scientific publications**

JRC Scientific and Technical Reports

## New plant breeding techniques

### State-of-the-art and prospects for commercial development

Maria Lusser, Claudia Parisi, Damien Plan and Emilio Rodríguez-Cerezo

EUR 24760 EN - 2011

JRC EUROPEAN COMMISSION

FEATURE

## Deployment of new biotechnologies in plant breeding

Maria Lusser[1,3], Claudia Parisi[1,3], Damien Plan[2] & Emilio Rodríguez-Cerezo[1]

**The first crops obtained through new plant breeding techniques are close to commercialization. Regulatory issues will determine the adoption of the techniques by breeders.**



The global food crisis of 2008 reminded us of the importance of innovation in agriculture to address global challenges such as population growth and climate change. The projections presented in a report of the Food and Agricultural Organization of the United Nations (proceedings of a high-level expert forum) show that feeding a world population of 9.1 billion people in 2050 would require raising overall food production by some 70% between 2005/07 and 2050 (ref. 1). Additionally, farmers will have to hit targets for reducing greenhouse gas emissions, improving water use efficiency and meeting the demands of consumers for healthful food and high-value ingredients. In this context, new plant breeding techniques are needed to contribute improvements in crop productivity and sustainability.

Clearly, an important aspect of technology adoption and dissemination is how such approaches relate to regulatory oversight and whether such breeding techniques fall under present rules for genetically modified organism (GMO) legislation. In the case of EU the issue is currently being analyzed[2–4]. Although studies analyzing new plant breeding techniques from the point of view of risk assessors and regulators are available[4–8], data are lacking on the refinement and/or maturation of technology and the extent of adoption in commercial breeding programs (and thus likely contribution to new crop varieties in the short or medium term).

To close this gap, we have conducted a study on new plant breeding techniques (beyond traditional genetic modification), under the aegis of the European Union's Joint Research Centre (JRC), that encompasses state-of-the-art technology and their prospects for commercial development, including zinc-finger nuclease (ZFN) technology[9,10], oligonucleotide-directed mutagenesis (ODM)[11,12], cisgenesis and intragenesis[13], RNA-dependent DNA methylation (RdDM)[14], grafting (on genetically modified (GM) rootstock)[15], reverse breeding[16] and agro-infiltration (encompassing agro-infiltration 'sensu stricto', agro-infection and floral dip)[17]. Our primary focus is on the current development status of these approaches, the main actors exploiting them in R&D (both public and private), the patenting landscape and the current use of these techniques by the commercial breeding sector. We also address the main drivers and constraints for the further adoption of these techniques. Finally, we analyze the possibilities for detecting and identifying crops produced using them (to fulfill possible regulatory requirements).

### Historical backdrop

Since the beginning of the twentieth century various tools have been introduced to broaden the possibilities for breeding new plant varieties. Chemical- and radiation-induced mutagenesis increases the frequency of genetic variations, and hybrid seed technology generates heterozygous plants with improved yield and disease resistance[18]. Applying the principles of cell biology and tissue culture—micropropagation, embryo rescue and double-haploid techniques—allows the rapid production of many uniform plants and the crossing of incompatible plants[18].

The latest wave of innovation in plant breeding, dating from the 1980s, came from 'modern biotech'. Molecular marker–assisted selection is now widely used to map and select commercially important agricultural traits[19]. Genetic modification, also known as genetic engineering, exploits recombinant DNA technology to expand the gene pool available to plant breeders. The earliest crops produced by genetic modification technologies (pest-resistant and herbicide-tolerant varieties) reached commercial cultivation in the mid-1990s and currently the global area sown with GM varieties measures over 148 million hectares[20].

In the past two decades, additional applications of biotech and molecular biology in plants have emerged, with the potential to further enlarge the plant breeder's toolbox. Several recently described techniques allow for site-directed mutagenesis of plant genes (to knock out or modify gene functions) and the targeted deletion or insertion of genes into plant genomes[5,9–12]. Another innovative trend is the use of transgenes solely as a tool to facilitate the breeding process.

In this application, transgenes are used in intermediate breeding steps and then selected for removal during later crosses, eliminating them from the final commercial variety. Among these tools are accelerated breeding techniques, where genes that promote early flowering are used to speed up breeding[21], and reverse breeding, a technique that produces homozygous parental lines from heterozygous elite plants[16].

The potential of these and other new techniques to produce innovative crop varieties will likely be affected by the regulatory framework of the regions where they are to be introduced. The application of modern biotech in the 1980s resulted in new forms of regulation and governance of certain plant breeding techniques (in particular genetic modification technologies) and of the release of GM crops into the environment. Various legal and regulatory approaches have been adopted worldwide, which include differing definitions of GM crops[22].

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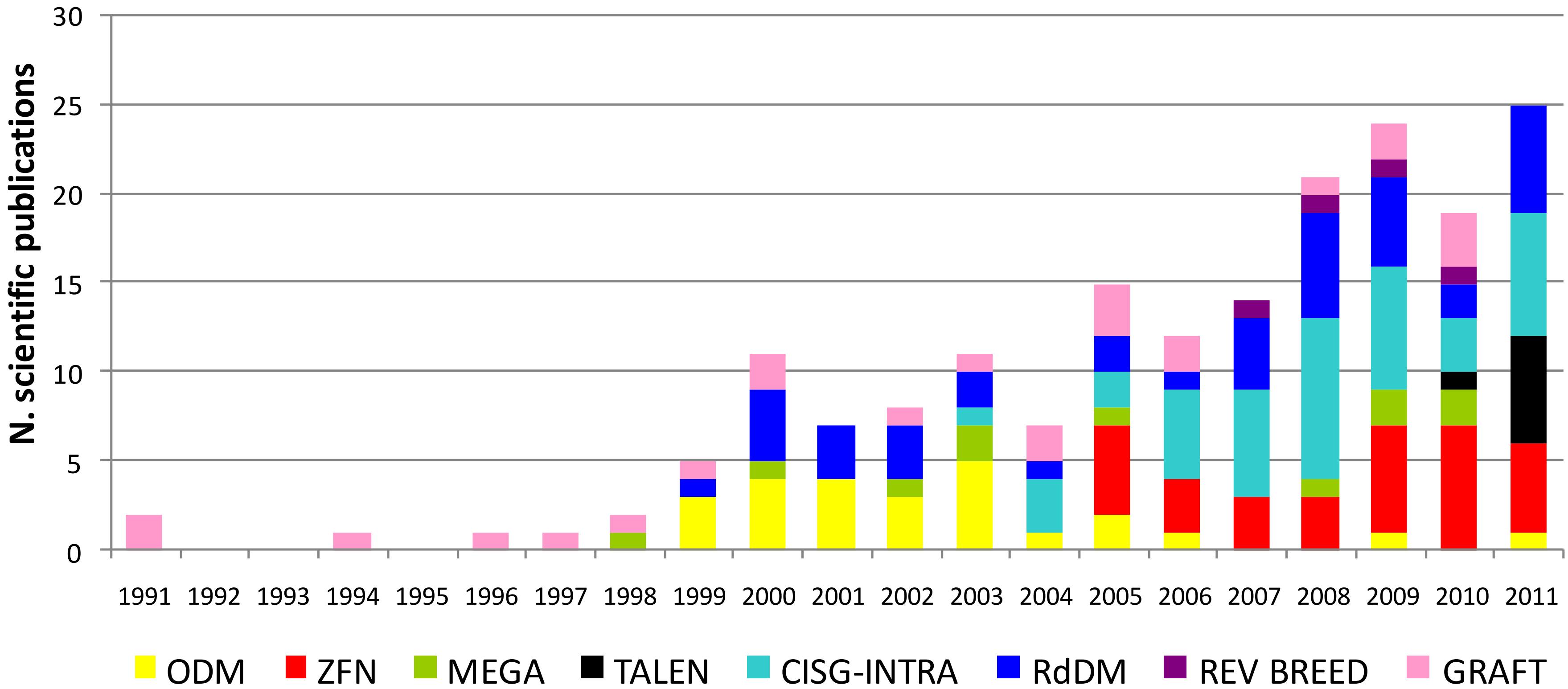
## Development over time of **scientific publications** on NPBTs

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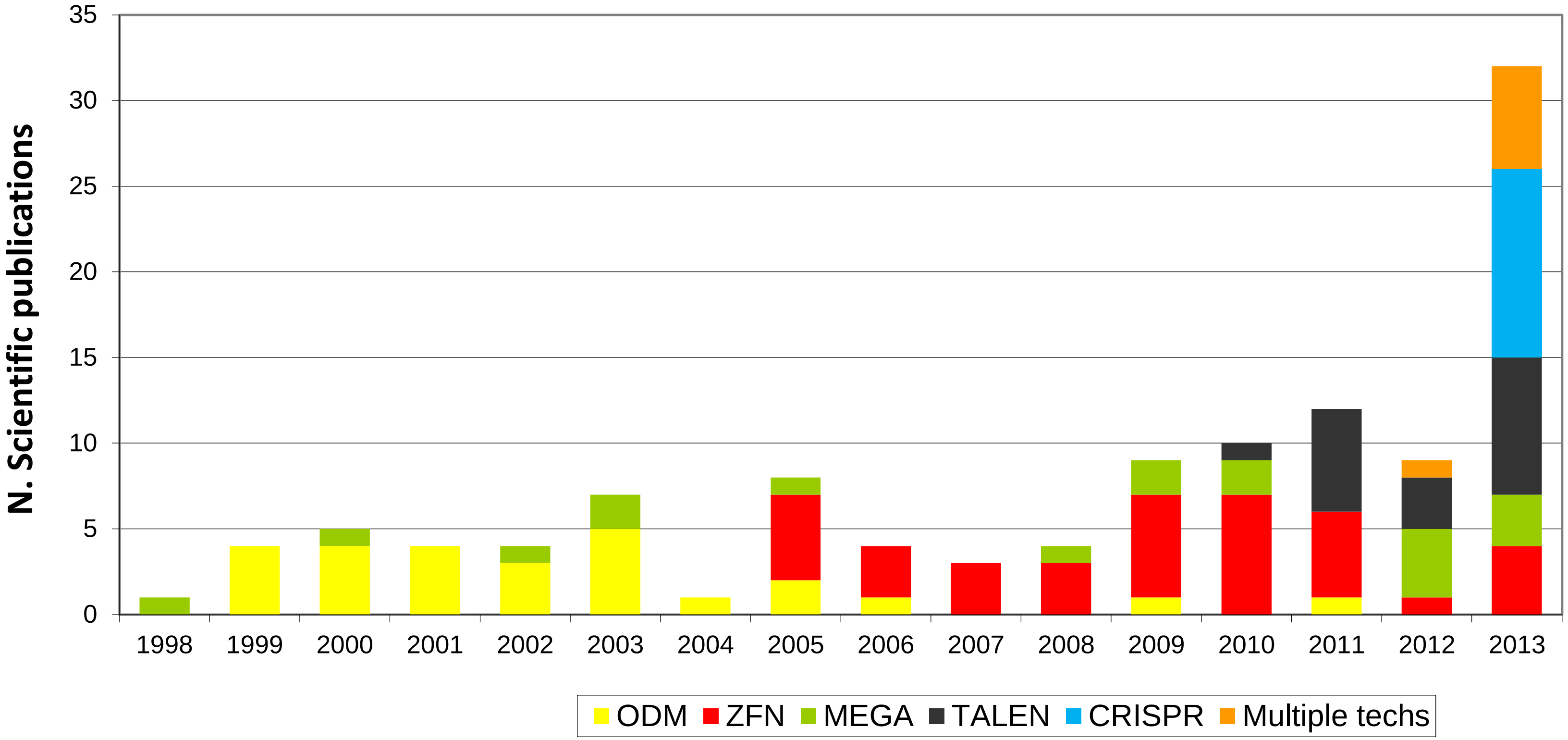
## Development over time of **scientific publications** on Site-Directed Mutagenesis




Multiple techs = papers or reviews about more than one technique of site-directed mutagenesis



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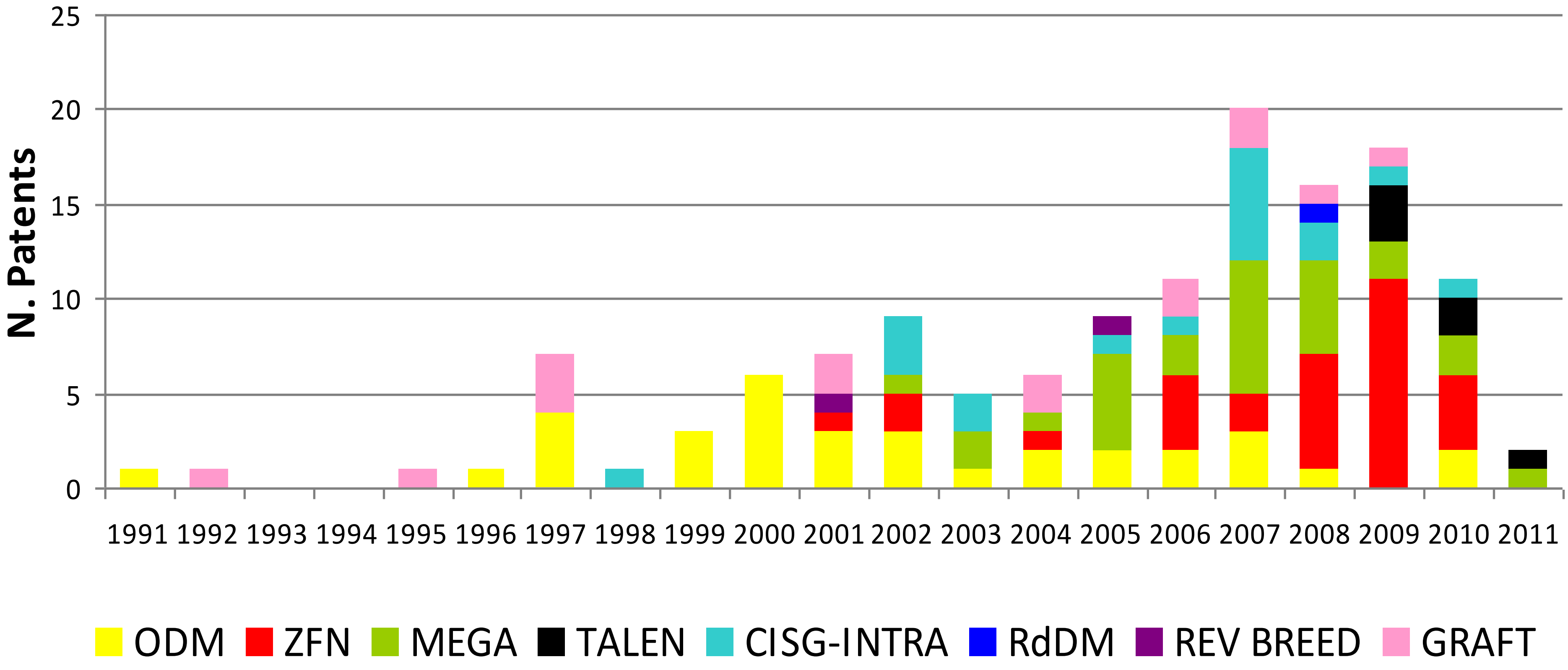
## Development over time of **patents** on NPBTs

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# Commercial development

| NPBT | Patent owner | Product name | Licensee | Plants |
|---|---|---|---|---|
| ODM | **Cibus Company (US)** | RTDS™ | | HT Oilseed rape (BASF), oil quality oilseed rape (BrettYoung), Flax (Flax Council of Canada), potato (NEU seed) |
| | **Keygene (NL)** | KeyBase™ | | HT tobacco, tomato and Petunia |
| ZFN | **Sangamo (US)** | EXZACT™ | **Dow** (exclusive) | HT maize, sugar beet (KWS Company), quality potato (Wageningen U.), lumber/paper prod. Trees (Oregon State U.) |
| | **Danziger Innovations (IL)** | MemoGene™ | | tobacco, tomato, Petunia, *Arabidopsis*, lettuce, *Agyranthemum* and *Populus tremula* |
| | **Toolgen (KR)** | GeneGripR | | *Arabidopsis* |
| MGN | **Cellectis Plant Sciences (FR)** | n.d. | **Monsanto** (non-excl.) | n.d. |
| | **Precision BioSciences (US)** | DNE | **Dupont, BASF** (non excl.) | Arabidopsis, tobacco, maize and more |
| TALEN | **Cellectis Plant Sciences (FR)** | n.d. | | n.d. |
| | **Two Blades Foundation** | n.d. | | n.d. |

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## **OECD Working Group on the Harmonisation of Regulatory Oversight in Biotechnology**

2014 questionnaire on NPBT employment among the delegations of the WG

1. Cisgenic apples with scab resistance (Switzerland, the Netherlands).
2. Fireblight resistant apples through accelerated breeding (Switzerland).
3. Citrus trees with transgenic rootstocks (Argentina).
4. Male-sterility technology in Maize (Argentina).
5. Cisgenic potatoes resistant to late blight (the Netherlands, Belgium, Ireland).
6. Different food crops developed via ODM (the Netherlands).
7. Trees with altered lignin composition developed via RNAi (Belgium).
8. Accelerated breeding using Apple latent spherical virus-based vectors (Japan).
9. Herbicide tolerant oilseed rape developed through ODM (UK).
10. Cereal varieties developed through site-directed nucleases (UK, Ireland).
11. Cisgenic maize lines that are drought and cold resistant (Mexico).
12. Cisgenic papaya resistant for a specific fungus (Mexico).
13. Applications of transplastomics/agroinfiltration for pharmac. purposes (Mexico).
14. Herbicide tolerant flax via ODM (Canada).
15. Queries submitted to US regulatory agencies (cisgenesis, ZFN, MGN, null-segregants).
16. Intragenic ryegrass with improved forage qualities (Australia).

| | |
|---|---|
| DETECTION | IDENTIFICATION |

**CISGENESIS/INTRAGENESIS**
**GM ROOTSTOCK**
**ZFN-3**

| | |
|---|---|
| DETECTION | ~~IDENTIFICATION~~ |

**ODM**
**ZFN-1,2**

| | |
|---|---|
| ~~DETECTION~~ | ~~IDENTIFICATION~~ |

**RdDM**
**REVERSE BREEDING**
**NON-GM SCION**

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# Conclusions

- The global GM crop pipeline has shown an evolution since 2008:
  - The number of authorised GM crops has more than doubled
  - Players from developing countries and from SMEs have a bigger role
- However:
  - The introduction of new crops and quality traits is happening slowly
  - Most players from developing countries only aim to cultivate and authorised their GM products domestically

- GM developers/breeders continue the trend of combining several traits by commercial stacking, which are becoming one of the dominant form of GM crops cultivated worldwide.

- NPBT, especially nuclease-directed mutagenesis, are emerging and reaching the market, but their products are in most cases indistinguishable from conventional (non-GM) crops from a detection point of view.

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# Thank you for your attention

For more information:

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