MON 1445

Roundup® Ready Cotton

Herbicide Tolerance

Key facts

Monsanto EMEA

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MON 1445 -Roundup Ready® cotton

Cotton

Worldwide, four *Gossypium* species are collectively known as cotton and are grown commercially. These include two diploid species (2n=2x=26) *G. arboreum* L. and *G. herbaceum* L., which evolved in Africa and the Middle East, and two allotetraploid species (2n=4x=52) *G. barbadense* and *G. hirsutum*, which evolved in the Americas. The major type of cotton being grown commercially around the world is the upland cotton *G. hirsutum*. *G. herbaceum* and *G. arboreum*, are of regional agronomic importance, mostly in areas not suited for *G. hirsutum* or *G. barbadense* (Southeast Asia and the dry, unproductive areas of India and Pakistan) and they comprise less than 4% of the total cotton produced globally. There are no close wild relatives of cotton in the EU.

The fiber, or lint, is used to make cloth—for towels, clothes, sheets, etc. The cottonseeds from the plant are crushed into cottonseed oil, which can be used in everyday items such as cooking oil and salad dressing, and into hulls and meal, which are used for livestock feed.

In 2013/2014 season, the major cottonseed oil, meal and oilseed producing countries in the world were China, India, Pakistan, Brazil and the US[1]. In the EU, cotton is commercially grown in Italy, Spain and Greece.

What is MON 1445 cotton?

Monsanto Company has developed a glyphosate-tolerant cotton product through *Agrobacterium tumefaciens*-mediated transformation. Genuity® Roundup Ready® cotton (hereafter referred to as MON 1445). The introduces *cp4 epsps* gene in MON 1445 results in expression of the 5 enolpyruvylshikimate-3 phosphate synthase (EPSPS) protein from *Agrobacterium tumefaciens* sp. strain CP4 (CP4 EPSPS), which confers tolerance to glyphosate, which is the active ingredient in Roundup® agricultural herbicides. MON 1445 also contains the *neomycin phosphotransferase II* (*nptII*) gene which provides a plant selectable marker; and the *3'(9)-O-aminoglycoside adenylyltransferase* (*aad*) gene, a bacterial selectable marker. The *cp4 epsps* and *nptII* genes are expressed in the plants; the *aad* gene-product is not produced in the plants as this gene is under the control of a bacterial promoter.

Use of MON 1445 enables the application of a Roundup® agricultural herbicide over the top of the cotton crop at later stages of development. This allows for effective weed control during crop production, because Roundup agricultural herbicides are highly effective against the majority of annual and perennial weeds that can be problematic during the later stages of crop development, with minimal risk of crop injury.

[1]Foreign Agricultural Service, Official USDA Estimates. http://apps.fas.usda.gov/psdonline/psdQuery.aspx.

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MON 1445: mode of action

Roundup herbicides contain the active ingredient glyphosate, a broad spectrum herbicide that acts via inhibition of the protein EPSPS. EPSPS is found naturally in all plants, fungi and bacteria and is important in the production of essential aromatic amino acids. Inhibition of EPSPS by glyphosate blocks the production of these amino acids, interfering with growth and ultimately leading to plant death (see Figure 1).

MON 1445 cotton plants contain a glyphosate tolerant EPSPS, isolated from the CP4 strain of the common soil bacterium *A. tumefaciens*. The presence of the glyphosate tolerant EPSPS ensures the continued function of the aromatic amino acid pathway, even in the presence of the herbicide glyphosate (see Figure 1). As a result of this genetic modification, MON 1445 is tolerant to glyphosate, allowing its over-the-top use for selective weed control in the crop.

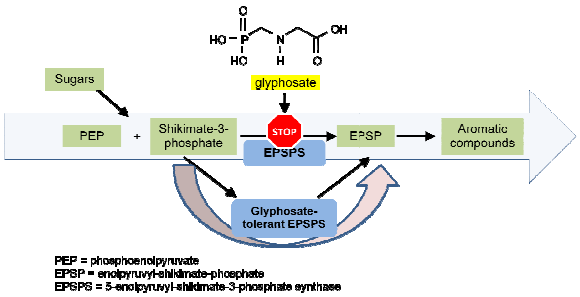

Figure 1: Schematic of the mode of action of the genetic modification in MON 1445

Worldwide plantings and regulatory status of MON 1445 cotton

In 2014, biotech cotton was planted to 25.1 million hectares, which is 68% of the 37 million hectares of global cotton (James, 2014). MON 1445 has received regulatory approvals for cultivation in Argentina, Australia, Brazil, Colombia, Mexico, Republic of South Africa and the US and additional import approvals in Canada, China, Colombia, EU, Japan, New Zealand, Korea, Mexico, the Philippines and Singapore[2]. MON 1445 is also part of stack applications. The first commercial plantings of MON 1445 cotton were in the US in 1997.

A stringent regulatory system for genetically modified crops in the EU

In the EU, the regulatory system for GM crops comprises several regulations and directives, including Directive 2001/18/EC for deliberate release of genetically modified organisms (GMOs) in the environment (repealing Directive 90/220/EEC) and Regulation (EC) No. 1829/2003 on genetically modified food and feed (replacing Regulation (EC) No. 258/97 on novel foods and novel food ingredients for GM products).

Regulation (EC) No 1829/2003 includes procedures for the authorization of deliberate release

[2]http://www.biotradestatus.com/ - Accessed 27 April 2015

(cultivation and/or import and processing), in addtion to Food and Feed use, according to the "one door, one key" principle.

A regulation on traceability and labeling of GMOs and products produced from GMOs (Regulation (EC) No. 1830/2003) entered into force on 18 April 2004. A regulation laying down the methods of sampling and analysis for the official control of feed as regards presence of genetically modified material for which an authorization procedure is pending or the authorisation of which has expired (Commission regulation (EU) No. 619/2011) entered into force on 24 June 2011.

Regulatory status of MON 1445 cotton in the EU

Foods and food ingredients

On 24 July 2002, Monsanto notified to the European Commission the placing on the market of foods and food ingredients derived from MON 1445, specifically cottonseed oil, according to Article 5 of Regulation (EC) No 258/97 on novel foods and food ingredients, on the basis of an opinion of substantial equivalence delivered by the UK Advisory Committee on Novel Foods and Processes (ACNFP). On 19 December 2002, the Commission forwarded the notification to the Member States and, this date can be considered as the date on which these foods and food ingredients were first placed on the EU market. As such, oil and its constituents produced from MON 1445 have been lawfully placed on the market according to Articles 8(1)(a) and 20(1)(a) of Regulation (EC) No 1829/2003.

Feed materials, feed additives and food additives

Feed materials, feed additives and food additives produced from MON 1445 were first placed on the market in the EU in 1997, following the commercial introduction of MON 1445 varieties in the US in 1997. Foods produced from cotton MON 1445 (food additives) were authorised under Directive 89/107/EEC, while feed produced from cotton MON 1445 (feed materials and feed additives) were subject to Directive 70/524/EEC.

After the date of entry into force of the Regulation (EC) 1829/2003, the products mentioned above were notified to the European Commission according to Articles 8(1)(a), 8(1)(b) or 20(1)(b) of this Regulation and subsequently included in the Community Register of GM food and feed.

Renewal application for use of food additives, feed material and feed additives

On 17 April 2007, Monsanto submitted a renewal application for use of food additives, feed material and feed additives produced from MON 1445 cotton as any other cotton under Regulation (EC) No 1829/2003 to European Food Safety Authority (EFSA) via the European Commission. On 16 June 2011, Monsanto added also the use of existing foods (oil) to the scope of the requested authorization.

The application received the reference number EFSA-GMO-RX-1445 and was declared valid on 03 July 2008. EFSA evaluated the application as well as Monsanto's additional information, scientific comments submitted by the Member States and relevant scientific publications. The EFSA published a positive scientific opinion on 16 December 2011 (adopted 30 November 2011) (EFSA, 2011), in which the EFSA concluded that "*MON 1445-derived products are as safe as products derived from the conventional counterpart in the context of their intended uses*".

Finally, on 16 March 2015, the European Commission presented the Draft Commission Implementing Decision authorizing the placing on the market of products produced from genetically modified cotton MON 1445, to the Standing Committee on Plants, Animals, Food and Feed (PAFF) for a vote. Since no qualifying majority was reached, the draft decision was passed to the Appeal Committee who met for a vote on 31 March 2015, again without reaching a qualified majority. The Appeal Committee forwarded the draft decision to the European Commission. The authorization was finally granted by the European Commission on 24 April 2015 (Commission Decision, 2015), 40 months after the EFSA opinion.

Traceability, labeling, unique identifier

Operators importing, handling or using MON 1445 derived foods and feeds in the EU should be informed of the legal obligations regarding traceability and labeling, laid down in Regulation (EC) No. 1830/2003. The unique identifier of MON 1445 cotton is MON-01445-2.

The validated methods, as well as the validation report for MON 1445, prepared by the CRL in collaboration with the European Network of GMO Laboratories (ENGL), were published on June 10, 2008 at the CRL website[3]. A report on the validation of the DNA extraction method for cotton seeds was also published on the same date.

Food, feed and environmental safety of MON 1445 cotton

Food and feed safety

The food and feed safety of MON 1445 cotton was established through:

- A detailed molecular characterization of the inserted DNA confirming a single copy to the T-DNA was inserted,
- An assessment of the toxic and allergenic potential of CP4 EPSPS and NPTII, based upon their long history of safe use, their rapid digestibility and their lack of toxicity or allergenicity, as demonstrated with bioinformatics as well as *in vitro* and *in vivo* safety studies with the protein,
- The compositional and nutritional analyses confirmed that MON 1445 is compositionally and nutritionally equivalent to, and as safe as, those of conventional cotton,
- A large margin of safety resulted from the low dietary exposure,
- An assessment showed that the intake resulting from consumption of foods derived from MON 1445 cotton does not raise nutritional concerns. The dietary safety of MON 1445 was further confirmed by repeat-dose animal feeding studies in catfish.

[3] http://gmo-crl.jrc.ec.europa.eu/StatusOfDossiers.aspx - accessed February 26, 2015

Further details on the safety of MON 1445 are available in a product safety summary on Monsanto's website[4].

Environmental safety

The environmental safety of MON 1445 was established through extensive field trials conducted in 1992, 1993, 1994, 1998 and 1999 in the US. All these field trials demonstrated that MON 1445 poses negligible risk to human health or to the environment.

Results showed that there are no unexpected changes in the phenotype or ecological interactions indicative of increased pest or weed potential of MON 1445 compared to the conventional cotton control. On the basis of these studies, it is possible to conclude that no differences in the mode or rate of reproduction, dissemination, survivability or other agronomic, phenotypic or ecological characteristics are expected in MON 1445 and that MON 1445 is not different in its phenotypic and agronomic behaviour relative to conventional cotton.

Moreover, considering the scope of the application, potential interactions of cotton MON 1445 with non-target organisms and the abiotic environment were not considered to be an issue due to the low level of exposure. The herbicide tolerance trait in MON 1445 cotton can be regarded as providing only a potential agronomic and selective advantage for this GM cotton plant where and when glyphosate herbicides are applied. Also, there are no close wild relatives of cotton in the EU.

In their scientific opinion on MON 1445, the EFSA concluded that "*cotton MON 1445-derived products are as safe as products derived from the conventional counterpart in the context of their intended uses.*"

MON 1445 cotton, the benefits

In countries where MON 1445 cotton is grown, a number of benefits for both farmers and the environment are expected. These include:

- Improved flexibility in weed control compared to herbicide programs used in conventional cotton, as specific pre-emergent herbicides that are used for prevention are replaced by a broad-spectrum post-emergent herbicide that can be used on an 'as needed' basis,
- Less labor required due to the elimination of hand weeding and high cost, early post-directed sprays which require special equipment,
- High compatibility with Integrated Pest Management and soil conservation techniques, resulting in a number of important environmental benefits including reduced soil erosion and improved water quality, improved soil structure with higher organic matter, improved wildlife habitat and improved carbon sequestration and reduced CO2 emissions.

Further reading

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EFSA, 2011. Scientific opinion on application EFSA-GMO-RX-MON1445 for renewal of the authorisation for continued marketing of cottonseed oil, food additives, feed materials and feed additives produced from cotton MON 1445 that were notified as existing products under Articles 8(1)(a), 8(1)(b) and 20(1)(b) of Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal, 9 (12), 1-28.

James C, 2014. Global status of commercialized biotech/GM crops: 2014. ISAAA, 49, Executive Summary.

[4] http://www.monsanto.com/products/documents/safety-summaries/cotton_pss.pdf. Accessed February 26, 2015.