MON 87705

High Oleic Soybean with increased monounsaturated fat and reduced polyunsaturated fat

Key Facts

Monsanto EMEA

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MON 87705 - High Oleic Soybean

Soybean, a key crop

Soybean (*Glycine max*) is a high-protein legume grown mainly as food for humans and livestock. It is the highest natural source of dietary fiber. Eight essential amino acids are found in soybeans, which are necessary for human nutrition and are not produced naturally in the body[1]. This crop is also used in industrial products including oils, soaps, cosmetics, resins, plastics, inks, solvents, and biodiesel.

The first record of domesticated soybean dates back to the 11th century BC in the eastern half of China where it was grown as food. Soybean was cultivated for the first time in Europe in the early 1700's and in North America in the early 1800's.

In 2013-2014, approximately 284 million metric tons (MMT) of soybean were produced in the world, which represents approximately 114 million hectares of soybean harvested globally. Significant areas of production included the US, Brazil, Argentina and China representing 26.9%, 26.5%, 17.2% and 5.7% of the global soybean hectares (Oil World Annual, 2014) respectively.

The EU is not a significant soybean producer. In 2013-2014, the soybean area harvested in the EU-28 accounted for approximately 504 thousand hectares distributed principally between Italy, Romania, Croatia, Hungary, Austria, France, and Slovakia (43.7%, 13.7%, 9.5%, 8.5%, 8.3%, 8.1% and 5.8% of the harvested area in Europe (Oil World Annual, 2014), respectively. Because of its low production and its high demand, especially for animal consumption, the EU is the world's largest importer of soybean meal and the second largest importer of whole soybeans, after China. In the period 2013-2014, the EU-28 expected to import 43.4 million metric tons of soybean meal and 13.9 million metric tons of whole soybeans (Oil World Annual, 2014) . Spain, Germany, the Netherlands, Italy and France are among the largest importer EU Member States (Oil World Annual, 2014).

Countries in North America and South America export large quantities of soybeans to the EU. In 2013-2014, about 41.6% of the EU imports came from Brazil, 23.7% from the US, 14.4% from Paraguay, and 8.3% from Canada.

What is MON 87705?

Monsanto Company has developed, through *Agrobacterium tumefaciens*-mediated transformation, biotechnology-derived soybean MON 87705 with an improved fatty acid (FA) profile that results in an oil that has improved suitability and stability for food and industrial uses.

Currently commodity soybean oil requires hydrogenation to improve its stability for use in many foods given its high proportion of polyunsaturated fatty acids. Hydrogenation results in the formation of trans fatty acids that pose known coronary health risks. As food companies reformulated foods to replace *trans* fat-containing hydrogenated oils with alternatives, they have faced challenges in finding high stability oils.

Using the extensive information known regarding the fatty acid biosynthetic pathway in soybean, MON 87705 was developed to selectively down-regulate, in seed, two key enzymes involved in fatty acid biosynthesis. As a result, MON 87705 soybean oil is lower in saturated fats (6% vs. 15% of total fatty acids) and higher in monounsaturated 18:1 oleic acid (76% vs. 23% FA), with an associated decrease in the polyunsaturated 18:2 linoleic acid levels (10% vs. 53% FA) relative to commodity soybean. In addition, soybean meal derived from MON 87705 contains very low residual oil and is unchanged in composition relative to commodity soybean meal. MON 87705 also contains the *5-enolpyruvylshikimate-3-phosphate synthase* gene derived from *Agrobacterium* sp. strain CP4 (*cp4 epsps*) encoding the CP4 EPSPS protein that is expressed throughout the plant conferring tolerance to glyphosate, the active ingredient in the Roundup® family of agricultural herbicides.

MON 87705: mode of action

The improved fatty acid profile in MON 87705 soybean oil is achieved through the use of endogenous soybean (*Glycine max* L.) gene segments configured to suppress *FATB* and *FAD2* gene expression. MON 87705 contains *FATB1-A* and *FAD2-1A* gene segments under the control of a seed promoter, limiting oil composition modification to this tissue. The assembled gene transcript has an inverted repeat that produces double stranded RNA (dsRNA) that, via the naturally occuring RNA interference (RNAi) pathway, suppresses endogenous *FATB* and *FAD2* gene expression, thereby producing the desired fatty acid phenotype (see Figure 1).

Acyl-acyl carrier protein (ACP) thioesterases (referred to herein as FATB enzymes) are localized in plastids and hydrolyze saturated fatty acids from the ACP-fatty acid moiety. The suppression of *FATB* results in a decrease in the transport of the saturated fats out of the plastid, thus retaining their availability for desaturation to 18:1 oleic acid (see Figure 1). Therefore, suppression of *FATB* decreases saturated fat content in the oil as well as increasing oleic acid. Subsequently, this increased amount of oleic acid is either delivered to the oil body or endoplasmic reticulum for further desaturation. Delta-12 desaturases (referred to as FAD2 enzymes) desaturate 18:1 oleic acid to 18:2 linoleic acid. The suppression of *FAD2* in soybean seed causes reduced desaturation of oleic to linoleic acid thus contributing further to the increase in oleic while reducing linoleic acid content in the oil. Therefore, the overall result of the suppression of these two enzymes is a reduction in saturated 16:0 palmitic and 18:0 stearic fatty acids,

[1]SoyStats. http://soystats.com/composition-of-a-soybean - accessed April 10, 2014

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an increase in monounsaturated 18:1 oleic acid, and lower levels of polyunsaturated 18:2 linoleic acid relative to commodity soybean.

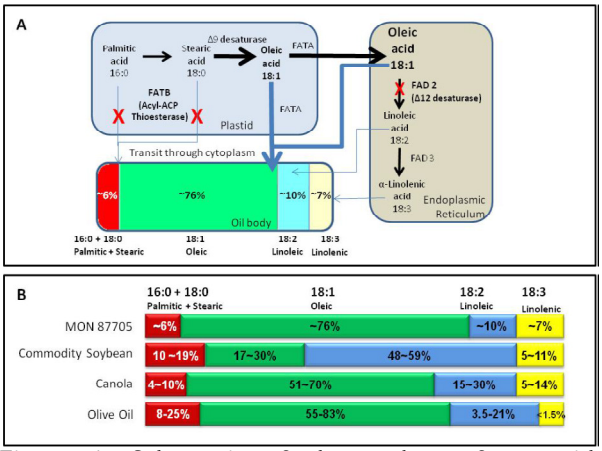

Figure 1. Schematic of the soybean fatty acid biosynthetic pathway and summary of modified fatty acid content in soybean oil derived from MON 87705
Panel A: Schematic of the soybean fatty acid biosynthetic pathway. The "X" symbols indicate suppression of endogenous *FATB* and *FAD2* in MON 87705 seeds.
Panel B: MON 87705 soybean oil compared to commodity soybean oil and other vegetable oils.

Worldwide plantings and regulatory status of MON 87705

Genetically modified crops protected against insect pests and/or tolerant to a specific herbicide are commercialized in the US by Monsanto since 1996. In 2014, approximately 182 million hectares of GM crops were grown worldwide (James, 2014). In the case of biotech soybean, it remained the principal biotech crop in 2014, occupying 90.7 million hectares (James, 2014).

MON 87705 has received regulatory approvals for cultivation in US and Canada and import in Australia/New Zealand, Colombia, Indonesia, Japan, Korea, Mexico, Singapore, and Taiwan[2].

MON 87705 will be bred into soybean varieties with diverse genetic backgrounds and combined using traditional breeding methods with other biotechnology-derived traits, including glyphosate-tolerance, to deliver the best agronomic platform to growers.
In order to derive commercial value from this product, the MON 87705 soybean crop will be grown and processed in an identity preserved manner in the northern US soybean growing regions and MON 87705 soybeans will be processed in dedicated oil processing facilities that will also be operated in an identity preserved manner and oil will be sold to food processors for food formulation.

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.

Regulation (EC) No 1829/2003 includes procedures for the authorization of deliberate release (cultivation and/or import and processing), in addition 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 87705 in the EU

On 18 February 2010, Monsanto submitted an application for import for food and feed use of MON 87705 soybean as any other soybean (excluding cultivation) under Regulation (EC) No 1829/2003 to European Food Safety Authority (EFSA) via the Dutch Competent Authority. The application received the reference number EFSA-GMO-NL-2010-78 and was declared valid on 13 August 2010. EFSA evaluated the application as well as Monsanto's additional information, scientific comments submitted by the Member States and relevant scientific publications. On 30 October 2012 (adopted 28 September 2012), the EFSA published a positive scientific opinion on the safety of MON 87705 (EFSA, 2012) which was complemented by an EFSA statement to cover the safety of MON 87705 soybean oil for commercial frying, published on 17 December 2013 (EFSA, 2013) (adopted 04 December 2013), which fulfils the requirements of article 6 and 18 of Regulation (EC) No 1829/2003.

EFSA concluded that MON 87705 "*is as safe as its conventional part with respect to potential effects on human and animal health and the environment in the context of its intended uses.*" In its opinion, EFSA also recommended a post market monitoring plan focused on the collection of consumption data.

On 23 May 2014, the European Commission presented the Draft Commission Implementing Decision authorizing the placing on the market of products containing, consisting of, or produced from genetically modified soybean MON 87705, to the Standing Committee on the Food Chain and Animal Health (SCFCAH) for a vote, but no qualifying majority was reached. After this vote, the draft decision was passed to the Appeal Committee who met for a vote on 10 June 2014, again without reaching a qualifying 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).

[2] http://www.biotradestatus.com/ - accessed April 13, 2015

Traceability, labelling, unique identifier

Operators handling or using MON 87705 and derived foods and feeds in the EU are required to be aware of the legal obligations regarding traceability and labelling of these products, laid down in Regulations (EC) No 1829/2003 and 1830/2003. The unique identifier for MON 87705 is MON-877Ø5-6.

In February 2010, a MON 87705-specific PCR-based detection method allowing the identification and quantification of MON 87705 was provided to the Joint Research Centre (JRC), acting as the Community Reference Laboratory (CRL). The validated methods, as well as the validation report for MON 87705, prepared by the CRL in collaboration with the European Network of GMO Laboratories (ENGL), were published on 02 February 2012 at the CRL website[3]. A report on the validation of the DNA extraction method for soybean seeds was also published on the same date.

Food, feed and environmental safety of MON 87705

Food and feed safety

The food and feed safety of MON 87705 was established based on the following:

- Soybean is a familiar crop that has a history of safe consumption, and serves as an appropriate basis of comparison,
- A detailed molecular characterization of the inserted DNA demonstrated a single, intact copy of the transgenic insert in a single locus within the soybean genome. This insert contains the *FATB* and *FAD2* suppression cassette and the *cp4 epsps* expression cassette,
- The inverted repeat encoded by the *FATB* and *FAD2* suppression cassette in MON 87705 does not code for any protein. The RNA-based suppression of *FATB* and *FAD2* soybean genes in MON 87705 is mediated by double stranded RNA (dsRNA) molecules. Double stranded RNAs are commonly used by eukaryotes, including plants, for endogenous gene suppression and pose no novel risks from a food, feed or environmental perspective. Nucleic acids, such as RNA, have a long history of safe consumption,
- The only introduced protein produced in MON 87705 is CP4 EPSPS. Data confirmed the CP4 EPSPS protein in MON 87705 is unlikely to be a toxin or allergen based on extensive information collected and evaluations performed. The CP4 EPSPS protein in MON 87705 has the same functional and enzymatic activity as the CP4 EPSPS in other Roundup Ready® crops previously assessed by the EFSA,
- A compositional assessment confirmed that, except for intended fatty acid changes, MON 87705 seed and forage are compositionally equivalent to seed and forage of conventional soybean. MON 87705 soybean oil does not contain any new fatty acids that are not already present in commodity soybean oil, and the fatty acid profile of MON 87705 soybean oil is similar to many other commercial oils currently available.
- A dietary risk assessment showed that the changes in fatty acid intake resulting from the replacement of conventional vegetable oils with oil from soybean MON 87705 do not raise nutritional concerns in the context of the intended uses. In addition to the extensive compositional analyses, the dietary safety of MON 87705 was further confirmed by repeat-dose animal feeding studies in the rat and in broiler chickens using MON 87705 soybean meal.

In its opinion (EFSA, 2012), EFSA concluded that *"soybean MON 87705 does not raise toxicity or allergenicity concerns with respect to the insertion and expression of new traits, and the altered fatty acid profile in the context of the intended uses as compared with its conventional counterpart and non-GM soybean reference varieties."*

Further details on the safety of MON 87705 are available in the EFSA's scientific opinions (EFSA, 2012, 2013).

Environmental safety

The environmental safety of MON 87705 was established through extensive field trials conducted in Chile in 2007/2008 and in the US in 2008, and various laboratory tests, demonstrating that MON 87705 poses negligible risk to human health or to the environment. Results from the phenotypic and agronomic assessments demonstrate that MON 87705 does not possess characteristics that would confer a plant pest risk compared to conventional soybean. Data on environmental interactions also indicate that MON 87705 does not confer any biologically meaningful increased susceptibility or tolerance to specific disease, insect, or abiotic stressors, or changes in agronomic and phenotypic characteristics.

Soybean does not have wild relatives in Europe to which the introduced trait could outcross. The likelihood of MON 87705 soybean spreading into the non-agronomic environment is negligible, since it is not more invasive in natural habitats than conventional soybean. Moreover, the scope of the authorization covers the processing and all uses as any other soybean, but excluding cultivation in the EU, and no deliberate release of the viable plant material in the EU environment is expected, thereby limiting the environmental exposure to accidental spillage only.

The herbicide tolerance trait in MON 87705 soybean can be regarded as providing only a potential agronomic and selective advantage for this GM soybean plant where and when glyphosate-based herbicides are applied. The expected changes in seed fatty acid composition in MON 87705 soybean resulting from the introduced FAD2-1A/FATB1-A suppression cassette are not known to provide a potential agronomic and selective advantage. Survival of soybean plants outside cultivation where glyphosate-based herbicides are applied is mainly limited by a combination of low competitiveness, absence of a

[3] http://gmo-crl.jrc.ec.europa.eu/StatusOfDossiers.aspx - accessed May 4, 2014

dormancy phase and susceptibility to plant pathogens and cold climatic conditions.

MON 87705 (High oleic) Soybean benefits

MON 87705 will deliver benefits to both farmers and the environment:

- The reduction in saturated fats and increased oxidative stability of MON 87705 soybean oil increases suitability for biodiesel and other industrial applications. Low saturated fats and high (>70%) oleic acid levels are key attributes for vegetable oils targeted for biodiesel and industrial uses because of improved cold weather performance, improved stability, and reduced nitrous oxide emissions.

References

Commission Decision, 2015. Commission Implementing Decision (EU) 2015/696 of 24 April 2015 authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean MON87705 (MON-877Ø5-6) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (notified under document C(2015) 2770). . Official Journal, L 112/60, 1.

EFSA, 2012. Scientific Opinion on application (EFSA-GMO-NL-2010-78) for the placing on the market of soybean MON 87705 genetically modified to contain stearidonic acid, for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. The EFSA Journal, 10 (10), 1-34.

EFSA, 2013. Statement complementing the scientific opinion on application EFSA-GMO-NL-2010-78 to cover the safety of soybean MON 87705 oil for commercial frying. The EFSA Journal, 11 (12), 1.

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

Oil World Annual, 2014. ISTA Mielke GmbH. 1.