

DECISION DOCUMENT

**Food and feed safety assessment of maize event
MON 89034 x TC1507 x NK603
OECD: MON-89034-3 x DAS-01507-1 x MON- 00603-6
(Includes all possible intermediate combinations)**



Directorate of Agrifood Quality

Office of Biotechnology and Industrialized Agrifood Products

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SUMMARY AND BACKGROUND

The process of food and feed risk assessment of a transformation event, product of modern biotechnology, is done by the National Service for Agrifood Health and Quality (SENASA), regulatory agency depending on the Ministry of Agriculture, Livestock and Fisheries.

The Directorate of Agrifood Quality of SENASA, is the area responsible for carrying out this function, counting for it with a Scientific Team and with the advice of a Technical Advisory Committee, composed of experts in several scientific disciplines, that represent the different sectors linked to production, industrialization, consumption, research and development of genetically modified organisms.

On November 18th 2009, the request by Monsanto Argentina S.A.I.C. and Dow AgroSciences Argentina S.A. was received for the assessment of food and feed aptitude of the transformation event MON89034 x TC1507 x NK603 (OECD: MON-89Ø34-3x DAS-Ø15Ø7-1 x MON- ØØ6Ø3-6), maize resistant to certain lepidopteran insects, tolerant to glifosate and to glufosinate-ammonium.

A review of the application was done in order to corroborate the compliance with Resolution SENASA N° 412/02, which is the legislation that establishes the criteria and requirements of food and feed risk assessment of genetically modified organisms.

The submitted information was analyzed in the first instance by the specific Technical Team, and then it was subject to the evaluation of the Technical Advisory Committee. Finally, the Directorate of Agrifood Quality evaluated again, in a third instance, and concluded in the current decision document.

EVALUATION

Maize MON89034 x TC1507 x NK603, resistant to certain lepidopteran insects, tolerant to glifosate and to glufosinate-ammonium, was evaluated following the guidelines from Resolution SENASA N° 412/02, on the “Fundamentals and Criteria for Evaluation of Food Derived from Genetically Modified Organisms”, the “Requirements and Standards of Procedures for the Food and Feed Risk Assessment of Food Derived from Genetically Modified Organisms”, and the “Required Information” for this assessment. The resolution considers the criteria provided by Codex Alimentarius FAO/OMS. The evaluation was carried out using the information submitted in the Annex III, together with the additional information requested and consultation with experts, to establish the food and feed aptitude for consumption.

1 – History of Use and Specification of the Transformation Event

Maize is the third cereal of importance at a global level, after rice and wheat. It was domesticated in pre-Columbian America more than 8000 years ago. It is commercially cultivated in several countries all around the world and it has a vast history of safe

consumption, with no reported cases of intoxication or allergies due to its reasonable consumption.

Maize MON89034 x TC1507 x NK603 plants have been obtained by conventional crossing, to express proteins Cry1F, Cry1A.105, Cry2Ab2 (from *Bacillus thuriangiensis*, proteins that confer resistance to certain lepidopteran insects); PAT (fosfinotricine acetiltransferase), protein that confers tolerance to glufosinate-ammonium, and protein CP4 EPSPS (derived from *Agrobacterium sp.* strain CP4) that confers tolerance to glifosate.

2 – Genetic stability and molecular characterization of the event.

The main genes of the event MON89034 x TC1507 x NK603 are: cry1A.105 that expresses the protein Cry1A.105, cry1F that expresses the protein Cry1F, cry2Ab2 that expresses the protein Cry2Ab2, pat that expresses the protein PAT and CP4 epsps that expresses the protein CP4 EPSPS.

The molecular analysis were opportunely completed to confirm the integrity and stability of the inserted DNA in the events MON89034, TC1507 and NK603. The molecular organization of the inserts was confirmed by Southern blot studies, demonstrating that the integrity of the inserts in each individual event is maintained in the stacked event. The patterns of hibridization (for the individual events and for the stacked event), and the inheritance of all the new genes were analyzed, confirming that they are inherited in a predictable pattern according to the principles of mendelian genetics.

3 –Pattern and levels of expression

The concentrations of the transgenic proteins in several plant tissues and growth stages of the crop, in the same location and during the same cultivation season were determined using ELISA techniques.

4 – Compositional Analysis

The applicant submitted information on the compositional analysis (during 2007 in 5 maize locations in USA) in grain and green tissue from maize hybrid plants that contain event MON89034 x TC1507 x NK603 compared to non transgenic maize (isogenic line and commercial hybrid).

A total of 62 components, 9 in forage and 53 in grain, were compared statistically using ANOVA. The studies show that, while some statistically significant differences were found, all analyzed values were within the range, and near the mean values of scientific literature (ILSI 2006), so the differences were not considered biologically relevant.

A 42 days broiler chicken study was analyzed to assess diets containing grain on event MON89034 x TC1507 x NK603 compared with the isoline and one commercial hybrid. The results of this study demonstrated that there was no adverse dietary effects on chickens fed on diets prepared with grain from maize MON89034 x TC1507 x NK603

compared with the diets prepared with grain from non transgenic maize, either by direct effect of the transgenic proteins in the diet, or as a result of unintentional compositional changes in the grain that could have generated toxic effects or alterations in its nutritional values.

It can be concluded that maize MON89034 x TC1507 x NK603 is substantially and nutritionally equivalent to its non transgenic counterpart and to conventional hybrids.

5 – Alergenicity

Homology with known allergenic proteins:

The allergenicity assessments of each of the introduced proteins were presented with the individual events and are kept current. The results of the submitted bioinformatic analysis show the absence of homologies of general sequence or immunologically relevant, when they were compared with pharmacologically active allergens or proteins.

The characteristics of molecular weight, concentration, simulated digestibility and thermostability of the new proteins were presented opportunely for each of the individual events. For none of the proteins evidence was found that can indicate them as potential allergens. These characteristics were not modified with the stacking of the events, therefore, according to the evaluated evidence, it is concluded that it is highly unlikely that maize event MON89034 x TC1507 x NK603 expresses allergenic substances.

6 – Toxicity.

The acute toxicity studies and bioinformatic studies of the proteins expressed were opportunely evaluated in the parental individual events, and are kept current. For this reason it is concluded that it is highly unlikely that maize event MON89034 x TC1507 x NK603 presents toxicological risks for human and animals.

7 – Metabolic interactions.

The evaluated studies indicate that the existence of effects of interaction (synergistic, antagonistic or enhancers) between the proteins when stacked is unlikely. Other evaluated evidences demonstrate that there are no phenotypic, compositional, nutritional nor bioefficacy changes, and that the proteins do not share metabolic pathways or modes of action.

Therefore, it is concluded that the existence of mechanisms of interaction between the genetic elements that affect the expression of the new proteins is unlikely.

8 – Conclusion

After a comprehensive assessment on the food and feed risk to the information submitted by Monsanto Argentina S.A.I.C. and Dow AgroSciences Argentina and taking into account that:

- The inheritance studies indicated that there is mendelian segregation.
- The proteins of new expression in grain are expressed at low levels.
- It is substantially and nutritionally equivalent to its non transgenic counterpart.
- No evidence was found on similarity or homology with known toxic proteins.
- Absence of evidence of expression of known allergenic substances for the proteins expressed in the stacked event.
- Studies that indicate that there are no effects of interaction between the proteins when the events are stacked were evaluated.
- The feeding study demonstrated that there are no adverse dietary effects.

It is concluded that maize event MON89034 x TC1507 x NK603 is substantially equivalent to its conventional counterpart, and it is as safe, and not less nutritious than the conventional commercial maize hybrids.

According to the previous descriptions, and based on the currently available scientific knowledge and on the internationally accepted requirements and criteria, there are no objections for the approval for human and animal consumption of maize MON89034 x TC1507 x NK603 and all the possible combinations of the individual events that compose it.

9 – Regulation and Recommendations

- Resolution SENASA N° 1265/99.
- Resolution SENASA N° 412/02.
- Principles for the risk analysis of food derived from modern biotechnology means (CAC/GL 44-2003).
- Guidelines for the assessment of the safety of food derived from plants with recombinant DNA (CAC/GL 45-2003).
- Consensus Document's for the work on the Safety of Novel Foods and Feeds (OECD).
- Resolution MAGyP N° 701/2011.
- Data Base ILSI 2007.
- Allergen Data Base (FARRP database).

Buenos Aires, 5/31/2012.