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KENMERK CGM/150928-01
ONDERWERP Advies hernieuwing van de vergunning voor import en verwerking van gg-maïs 1507

Geachte mevrouw Mansveld,

Naar aanleiding van een aanvraag voor het hernieuwen van de vergunning voor import en verwerking van de genetisch gemodificeerde maïslijn 1507 ingediend door Pioneer Hi-Bred International Inc. en Dow Agrosciences LLC (EFSA/GMO/RX/001) deelt de COGEM u het volgende mee.

Samenvatting:

De COGEM is gevraagd om te adviseren over de hernieuwing van de vergunning voor import en verwerking van de genetisch gemodificeerde (gg-) maïslijn 1507. De eerdere vergunning is in 2006 voor een periode van tien jaar verleend.

Maïslijn 1507 brengt de *pat* en *cryIF* genen tot expressie en is daardoor tolerant voor glufosinaat-ammonium bevattende herbiciden en resistent voor bepaalde insecten uit de orde van de Lepidoptera.

De vergunningaanvraag bevat onder andere geactualiseerde bioinformatische analyses, de resultaten van de verplichte 'post-market environmental monitoring' (PMEM) die de afgelopen negen jaar is uitgevoerd, en een overzicht van de wetenschappelijke literatuur die tussen 2009 en 2015 is verschenen en relevant is voor deze vergunningaanvraag. De COGEM heeft deze informatie geanalyseerd en geen aanwijzingen gevonden dat import en verwerking van gg-maïs 1507 een risico voor mens en milieu zou kunnen vormen.

Verwilderde maïsplanten zijn in Nederland nooit waargenomen en opslag van maïsplanten is in Nederland nagenoeg uitgesloten. Er is bij de verplichte PMEM geen verwilderde 1507 maïs opgemerkt in Europa. Bovendien kunnen de ingebrachte sequenties zich niet naar andere soorten verspreiden, omdat er in Europa geen wilde verwanten van maïs voorkomen.

Gezien het bovenstaande acht de COGEM, in overeenstemming met haar eerdere advies, de risico's van import en verwerking van maïslijn 1507 voor mens en milieu verwaarloosbaar klein.



De door de COGEM gehanteerde overwegingen en het hieruit voortvloeiende advies treft u hierbij aan als bijlage.

Hoogachtend,

Prof. dr. ing. Sybe Schaap
Voorzitter COGEM

c.c. Drs. H.P. de Wijs, Hoofd Bureau ggo
 Mr. J.K.B.H. Kwisthout, Ministerie van IenM

Renewal of the authorisation for import and processing of genetically modified maize line 1507

COGEM advice CGM/150928-01

Introduction

Maize 1507 is a genetically modified maize line that expresses the *pat* and *cry1F* genes. As a result, it is tolerant to glufosinate-ammonium containing herbicides and resistant to certain lepidopteran insects, such as the European corn borer (*Ostrinia nubilalis*) and the Mediterranean corn borer (*Sesamia nonagrioides*).

Maize 1507 is authorised for import and processing in 49 countries. Since 2006, maize 1507 is authorised to be used as any other maize in the European Union (EU), with the exception of cultivation.^{1,2,3} Authorisations of GM food and feed are granted for a period of ten years. After this period the authorisation has to be renewed. In 2011, the authorisation for continued marketing of existing feed products produced from 1507 maize was renewed.⁴ The current application concerns the renewal of the authorisation of food and feed produced from 1507 and its import and processing.

In the USA, commercial cultivation of maize 1507 started in 2003. Cultivation of 1507 maize is currently authorised in ten other countries (amongst others in Canada, Argentina and Japan). In 2003, the applicant submitted an application for cultivation of maize 1507 in the EU. A decision on an authorisation for cultivation is still pending.

COGEM has been asked to advice on the renewal of the authorisation of food and feed produced from maize 1507 and its import and processing. To draft this opinion, COGEM analysed the information in the application for renewal of the authorisation, including the scientific publications that were identified in the literature search carried out by the applicant.

Description of maize 1507

Maize 1507 was generated by particle bombardment with the linear DNA fragment PHI8999A containing two expression cassettes:

- 1) a synthetic version of the truncated *cry1F* gene derived from *Bacillus thuringiensis* subsp. *aizawa* under the regulation of the ubiquitin gene 1 (*ubiZM1*) promoter (including the 5' untranslated region and intron) derived from *Zea mays* and the ORF25PolyA terminator from *Agrobacterium tumefaciens* pTi15955
- 2) a synthetic plant optimised version of the *pat* gene derived from *Streptomyces viridochromogenes* strain Tü494 under the regulation of the 35S promoter and terminator sequences from *cauliflower mosaic virus*.

Maize 1507 has a single integration locus located at chromosome 2 of the maize genome that consists of the full PHI8999A DNA fragment used for transformation and several additional fragments.

According to the applicant, the integration locus contains the following genetic elements:

- a *cryIF* fragment (335 bp)
- maize genomic sequence (338 bp)
- a *pat* fragment (201 bp)
- an inverted *pat* fragment (138 bp)
- a *cryIF* fragment (15 bp)
- a fragment of PHI8999A (118 bp)
- the full length insert of PHI8999A containing the above described *cryIF* and *pat* expression cassettes (6,186 bp)
- the inverted ORF25 terminator (503 bp)
- a polylinker region from PHI8999A (45 bp)
- maize genomic sequence (520 bp)
- a *pat* fragment (188 bp)
- maize genomic sequence (81 bp)

Previous COGEM advices

In 2003, COGEM issued two opinions on 1507 maize. COGEM considered the environmental risks associated with import and processing, and those associated with cultivation in the Netherlands to be negligible.^{5,6}

In addition, in the following years the environmental risks associated with import and processing of several stacked events with maize 1507 as one of the parental lines, such as Bt11x59122xMIR604x1507xGA21⁷ and MON87427xMON89034x1507xMON88017x59122,⁸ were deemed to be negligible by COGEM.

Food/ feed assessment

Since 2008, COGEM abstains from giving advice on the potential risks of incidental consumption since a food/feed assessment is already carried out by other organisations.⁹ This application is submitted under Regulation (EC) 1829/2003, therefore a food/feed assessment is carried out by EFSA and national organisations involved in the assessment of food safety. In the Netherlands, a food/feed assessment for Regulation (EC) 1829/2003 applications is carried out by RIKILT. The outcome of the assessment by these organisations (EFSA, RIKILT) was not known upon the completion of this advice.

New information

Molecular characterisation

In 2009, a single nucleotide difference in the 35S CaMV promotor sequence was reported that was not detected hitherto.¹⁰ This mutation was most likely introduced during the transformation process

as it is not present in the PHI8999A DNA fragment used for transformation. In the same year, the sequence analysis was redone and four other single nucleotide differences were reported. These differences were present in both the 1507 insertion sequence and the PHI8999A DNA fragment used for transformation. The applicant concludes that these were misreads of the DNA sequencing results caused by the sequence technology that was used, which was more prone to errors than the sequence technology which is currently being used.

In the current application, a renewed bioinformatic analysis of the integration locus and the flanking regions was provided using the corrected DNA sequence. The analysis showed that no endogenous maize genes were disrupted by the integration locus (the full length PHI8999A insert and several fragments). The sequences between the full length PHI8999A insert and the PHI8999A fragments align to sequences from maize chromosomes and maize chloroplast sequences. The applicant states that these sequences correspond to maize genomic DNA. Some of the maize sequences present between the PHI8999A fragments align to hypothetical proteins, but according to the applicant it is unlikely that they are expressed because regulatory elements and translational start sites are not located adjacent to these sequences.

The nucleotide sequence of the entire integration locus and its flanking genomic DNA (spanning the junction sites) was translated *in silico* in all six reading frames to generate putative protein sequences which were subsequently analysed for homology to putative allergens and toxins. No similarities to known putative allergens and toxins were identified.

Post-market environmental monitoring

As required by the EU authorisation, the potential occurrence of unexpected adverse effects from import and processing of 1507 maize was monitored since March 2006. Annual monitoring reports and a summary of the monitoring results from March 2006 to February 2015 were submitted. No adverse effects or incidents have been reported.

As part of the required post-market environmental monitoring, the applicant also performed a literature search on scientific publications published from 2009 to 2015 and relevant to the application. These publications did not contain information indicating that import and processing of 1507 maize could pose an environmental risk.

Conclusion

Maize is a domesticated crop that has lost the ability to survive in the wild. In the Netherlands, volunteers are rare and establishment of maize plants in the wild has never been observed.

There is no indication that the traits introduced in 1507 maize, i.e. tolerance to glufosinate-ammonium containing herbicides and resistance to certain lepidopteran insects, increases the potential of 1507 maize to establish feral populations. In the USA, maize 1507 has been cultivated since 2003. Feral populations of 1507 maize have not been reported. In an experiment, 1507 maize plants were not harvested and left on the field. Volunteer maize plants grew from seeds from fallen ears, but were absent after nine months.¹¹

Introgression of the introduced sequences into closely related species cannot occur, as wild relatives of maize are not present in Europe.

In 2003, COGEM advised on the original application for import and processing of 1507 maize and concluded that the environmental risks associated with import and processing of this maize line were negligible. The current application concerns the renewal of this authorisation and contains amongst other things updated bioinformatic analyses, the results from the post-market environmental monitoring that was carried out from March 2006 to February 2015, and results of literature searches on scientific publications that appeared from 2009 to 2015 and are relevant to this application.

COGEM analysed the above mentioned information and did not identify information revealing potential environmental risks of import and processing of 1507 maize. Therefore, COGEM's previous conclusion that import and processing of this maize line poses a negligible risk to the environment remains valid.

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