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**KENMERK** CGM/180430-02  
**ONDERWERP** Advies import en verwerking van gg-mais  
Bt11xMIR162xMIR604x1507x5307xGA21

Geachte mevrouw Van Veldhoven,

Naar aanleiding van een vergunningaanvraag voor import en verwerking van genetisch gemodificeerde maïs Bt11xMIR162xMIR604x1507x5307xGA21 (EFSA/GMO/DE/2011/103), ingediend door Syngenta, deelt de COGEM u het volgende mee.

**Samenvatting:**

De COGEM is gevraagd te adviseren over de mogelijke milieurisico's van import en verwerking van de genetisch gemodificeerde (gg-) maïs Bt11xMIR162xMIR604x1507x5307xGA21 en alle subcombinaties daarvan. In deze gg-maïs komen de genen *pat* en *mepsps* tot expressie, waardoor de plant tolerant is voor bepaalde herbiciden. Ook komen de genen *cry1Ab*, *vip3Aa20*, *mcry3A*, *cry1F* en *ecry3.1Ab* tot expressie, waardoor de plant resistent is tegen bepaalde plaaginsecten die behoren tot de vlinder- en keverachtigen. De hybride bevat ook het *pmi* gen dat ervoor zorgt dat na het transformeren gg-plantencellen gemakkelijk geselecteerd kunnen worden.

Verwildering van maïsplanten is in Nederland nooit waargenomen. Maïsplanten uit gemorst zaad (opslagplanten) worden hier nauwelijks aangetroffen. Bovendien zijn er in Nederland geen wilde verwanten van maïs aanwezig, waardoor de ingebrachte sequenties niet naar andere soorten kunnen verspreiden.

De moleculaire karakterisering van Bt11xMIR162xMIR604x1507x5307xGA21 voldoet aan de eisen van de COGEM. Er zijn geen redenen om aan te nemen dat expressie van de ingebrachte genen ervoor zorgt dat deze gg-maïs zou kunnen verwilderen.

Gezien het bovenstaande acht de COGEM de milieurisico's van de import en verwerking van de gg-maïs Bt11xMIR162xMIR604x1507x5307xGA21, en subcombinaties hiervan, verwaarloosbaar klein.

Omdat een voedselveiligheidsbeoordeling door andere instanties wordt uitgevoerd, heeft de COGEM bij deze vergunningaanvraag de risico's van incidentele consumptie niet beoordeeld.



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 IenW  
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## **Import and processing of genetically modified maize Bt11xMIR162xMIR604x1507x5307xGA21**

### **COGEM advice CGM/180430-02**

- The present application (EFSA/GMO/DE/2011/103) concerns the authorisation for import and processing for use in feed and food of genetically modified (GM) maize Bt11xMIR162xMIR604x1507x5307xGA21 and GM maize consisting of sub-combinations of the parental GM maize lines;
- Maize Bt11xMIR162xMIR604x1507x5307xGA21 was produced by conventional crossbreeding of the six GM parental maize lines;
- Previously, COGEM advised positively on the import and processing of all six parental lines;
- The molecular characterisation of Bt11xMIR162xMIR604x1507x5307xGA21 has been updated and meets the criteria of COGEM;
- The updated molecular characterisation does not provide indications for potential environmental risks;
- The GM maize expresses the genes *cry1Ab*, *vip3Aa20*, *mcry3A*, *cry1F*, *ecry3.1Ab*, *pat*, *mepsps* and *pmi*;
- It is resistant to certain lepidopteran and coleopteran insects, tolerant to glyphosate and glufosinate-ammonium containing herbicides, and able to use mannose as a carbon source;
- In the Netherlands, feral maize populations have never been observed and the appearance of volunteers is rare;
- In the Netherlands, wild relatives of maize are absent and hybridisation of maize with other species is therefore not possible;
- There are no indications that the introduced traits allow Bt11xMIR162xMIR604x1507x5307xGA21 to survive in the Netherlands;
- There are no indications that Bt11xMIR162xMIR604x1507x5307xGA21 could establish feral populations in the Netherlands;
- COGEM is of the opinion that import and processing of maize Bt11xMIR162xMIR604x1507x5307xGA21, and GM maize consisting of sub-combinations of its parental GM maize lines poses a negligible risk to the environment in the Netherlands;
- COGEM abstains from giving advice on the potential risks of incidental consumption since a food/feed assessment is carried out by other organisations.

## 1. Introduction

The present application (EFSA/GMO/DE/2011/103) filed by Syngenta concerns import and processing of Bt11xMIR162xMIR604x1507x5307xGA21 maize and genetically modified (GM) maize consisting of sub-combinations of the parental GM maize lines. The GM maize was produced by conventional crossbreeding of six genetically modified (GM) parental maize lines. It expresses the *pat* and *mepsps* genes conferring tolerance to glyphosate and glufosinate-ammonium containing herbicides, and expresses the *cry1Ab*, *vip3Aa20*, *mcry3A*, *cry1F* and *ecry3.1Ab* genes resulting in resistance to certain lepidopteran and coleopteran insects. In addition, it expresses the *pmi* gene. As a result transformed plant cells are able to use mannose as a sole carbon source.

Parental lines Bt11<sup>1</sup>, MIR162<sup>2</sup>, MIR604<sup>3</sup>, 1507<sup>4</sup> and GA21<sup>5</sup> have been authorised for import and processing for use in food and feed in the European Union. Several stacked events have also been authorised for import and processing for use in food and feed in the European Union.<sup>(e.g. 6)</sup> The parental line 5307 has been assessed for import and processing for use in food and feed. In 2015 EFSA has issued an inconclusive scientific and overall opinion, because it could not conclude on the safety of the eCry3.1Ab protein due to an inadequate toxicity study provided.<sup>7</sup> Recently, EFSA assessed a supplementary 28-day toxicity study in mice on the eCry3.1Ab protein and concluded that the toxicity study did not show adverse effects. Taking into account the previous assessment and the new information EFSA concluded that maize 1507 is as safe and nutritious as its conventional counterpart in the scope of the application.<sup>8</sup>

## 2. Previous COGEM advices

COGEM has previously advised positively on import and processing of all six parental lines: Bt11<sup>9,10</sup>, MIR162<sup>11</sup>, MIR604<sup>12</sup>, 1507<sup>13,14,15</sup>, 5307<sup>16</sup> and GA21<sup>17,18</sup>. COGEM also advised positively on the import and processing of several stacked events including Bt11xMIR162xMIR604xGA21<sup>19</sup>, Bt11xMIR162x1507xGA21<sup>20</sup> and Bt11x59122xMIR604x1507xGA21<sup>21</sup>. The environmental risks of import and processing were considered negligible.<sup>9,11,12,13,14,15,16,17,18,19,20,21</sup>

## 3. Environmental risk assessment

Potential environmental risks of Bt11xMIR162xMIR604x1507x5307xGA21 maize and of GM maize consisting of sub-combinations of its parental GM maize lines are assessed as part of the environmental risk assessment carried out by COGEM.

### 3.1 Aspects of the wild-type crop

Maize (*Zea mays*) is a member of the grass family *Poaceae*. It is a highly domesticated crop originating from Central America, but nowadays cultivated globally. Maize is wind pollinated,<sup>22,23</sup> and has both male and female flowers that are spatially separated. Female flowers are not attractive to insect pollinators, because they do not produce nectar. Insect pollination of maize is probably highly limited but cannot be excluded.<sup>24</sup>

Recently the wild relative of maize teosinte, has been reported as a weed in maize fields in Spain<sup>25,26,27</sup> and France.<sup>28,29</sup> In the Netherlands, no wild relatives of maize are present and hybridisation with other species cannot occur.

Maize requires warm conditions in order to grow and does not tolerate prolonged cold and frost.<sup>24,30</sup> In cultivation areas with warm climatic conditions, the appearance of volunteers can occur the year following maize cultivation due to spilled cobs or kernels. However, these volunteers are usually killed by common mechanical pre-planting soil preparation practices.<sup>24</sup>

Maize is very sensitive to weed competition.<sup>31</sup> During the long process of domestication, maize has lost the ability to persist in the wild.<sup>23</sup> A soil seed bank, small seeds, and an extended period of flowering and seed production are characteristics often observed in persistent weeds.<sup>32</sup> Maize lacks all these characteristics. After ripening, the seeds (the kernels) adhere to the cob and do not shatter naturally.<sup>24,33</sup> Consequently, seed dispersal is severely hampered.

During field observations in Austria some volunteers and maize plants were observed in non-agricultural habitats.<sup>34</sup> In the Netherlands, the appearance of volunteers is very rare, although maize plants occasionally have been observed outside agricultural fields.<sup>35</sup> COGEM is not aware of any reports of feral maize populations in the Netherlands or elsewhere in Europe.

**Conclusion:** In the Netherlands, feral maize populations do not occur and hybridisation of maize with other species is not possible.

### 3.2 Description of the introduced genes and traits

Introduced genes	Encoded proteins	Traits
<i>cry1Ab</i>	A variant of the Cry1Ab protein from <i>Bacillus thuringiensis</i> subsp. <i>kurstaki</i> <sup>36</sup>	Resistance to certain lepidopteran insects
<i>cry1F</i>	A variant of the Cry1F protein originating from <i>B. thuringiensis</i> subsp. <i>aizawa</i> <sup>37</sup>	Resistance to certain lepidopteran insects
<i>ecry3.1Ab</i>	A chimera of a variant of the Cry3A protein from <i>B. thuringiensis</i> subsp. <i>tenebrionis</i> (mCry3A), <sup>38,39,40</sup> and the Cry1Ab protein from <i>B. thuringiensis</i> subsp. <i>kurstaki</i> <sup>38,41,42,43</sup>	Resistance against certain coleopteran insects
<i>mcry3A</i>	A variant of the Cry3A protein from <i>B. thuringiensis</i> subsp. <i>tenebrionis</i> <sup>38,44,45</sup>	Resistance against certain coleopteran insects
<i>mepsps</i>	Modified 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) originating from <i>Zea mays</i> <sup>46</sup>	Tolerance to glyphosate containing herbicides, because of a decreased binding affinity for glyphosate
<i>pat</i> (two copies)	Variant of phosphinothricin N-acetyltransferase (PAT) originating from <i>Streptomyces viridochromogenes</i> strain Tü 494 <sup>47,48</sup>	Tolerance to glufosinate-ammonium containing herbicides

Introduced genes	Encoded proteins	Traits
<i>pmi</i> (three copies), also known as <i>manA</i>	Two variants (PMI and MIR604 PMI) with two amino acid difference of the phosphomannose isomerase (PMI) enzyme derived from <i>E. coli</i> . <sup>49</sup>	Enables transformed plant cells to use mannose as a sole carbon source
<i>vip3Aa20</i>	Variant of a native vegetative insecticidal protein (Vip) class A, subclass a, (Vip3Aa20) originating from <i>B. thuringiensis</i> strain AB88 <sup>38,50</sup>	Resistance against certain lepidopteran insects
See references for a detailed description of the traits		

### 3.3 Molecular characterisation

Previously, COGEM evaluated the molecular characterisation of each parental line and considered these to be adequate.<sup>9,10,11,12,15,16,18</sup>

The applicant confirmed by Southern blot analysis that the hybrid contained the parental transgenic inserts of Bt11, MIR162, MIR604, 1507, 5307 and GA21, and that no rearrangements of these inserts occurred.

The applicant also updated the bioinformatic analyses of the inherited inserted elements, and the sequences spanning the insertion sites at the 5' and 3' flanking regions using recent databases.

According to the applicant, no essential endogenous genes were disrupted at the insertion sites, and the putative products of the open reading frames spanning the 5' and 3' junctions of the inserts, did not generate any protein sequence similarity with known allergens, toxins or other biologically active proteins.

The molecular characterisation was conducted according to the criteria previously laid down by COGEM.<sup>51</sup> The results from the updated molecular characterisation do not provide indications that Bt11xMIR162xMIR604x1507x5307xGA21 could pose a risk to the environment.

**Conclusion:** The molecular characterisation of maize Bt11xMIR162xMIR604x1507x5307xGA21 is adequate and no indications for potential environmental risks were identified.

### 3.4 Phenotypic and agronomic characteristics

Previously, COGEM evaluated the phenotypic and agronomic characteristics of each parental line of Bt11xMIR162xMIR604x1507x5307xGA21, and found no deviations influencing the outcome of the environmental risk assessment.

The applicant analysed the phenotypic and agronomic characteristics of Bt11xMIR162xMIR604x1507x5307xGA21 and noted that most agronomic characteristics did not differ from those in the non-GM near-isogenic line. When differences were observed, they were within ranges considered to be normal for conventional maize. The results of the phenotypic evaluation do not give reason to assume that the GM maize could pose an environmental risk. According to the applicant the results of the field trials support the conclusion that from an agronomic and phenotypic point of view, Bt11xMIR162xMIR604x1507x5307xGA21 is equivalent

to conventional maize, except for the inherited lepidopteran and coleopteran protection and the tolerance to glyphosate and glufosinate-ammonium herbicides.

In conclusion, COGEM is of the opinion that there are no reasons to assume that the introduced traits in Bt11xMIR162xMIR604x1507x5307xGA21 allow the GM maize to survive or establish in the Dutch environment.

**Conclusion:** There are no indications that the introduced traits allow Bt11xMIR162xMIR604x1507x5307xGA21 to survive in the Netherlands. Bt11xMIR162xMIR604x1507x5307xGA21 does not have an increased potential for the establishment of feral populations in the Netherlands.

#### **4. Food/feed assessment**

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, RIKILT carries out a food and/or feed assessment for Regulation (EC) 1829/2003 applications. The outcome of the assessment by other organisations (EFSA, RIKILT) was not known when this advice was completed.

#### **5. Post-market environmental monitoring (PMEM)**

The applicant supplied a general surveillance plan as part of the PMEM. COGEM has published several recommendations for further improvement of the general surveillance (GS) plan,<sup>52,53</sup> but considers the current GS plan adequate for the import and processing of maize Bt11xMIR162xMIR604x1507x5307xGA21.

#### **6. Overall conclusion**

There are no indications that expression of the introduced traits will alter the fitness of maize Bt11xMIR162xMIR604x1507x5307xGA21 under natural conditions. COGEM is of the opinion that import and processing of Bt11xMIR162xMIR604x1507x5307xGA21 maize and GM maize consisting of sub-combinations of its parental GM maize lines poses a negligible risk to the environment in the Netherlands.

COGEM abstains from giving advice on the potential risks of incidental consumption since other organisations carry out a food/feed assessment.

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