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Geachte Voorzitter,

In het debat met uw Kamer op 27 januari 2009 over biotechnologie heb ik toegezegd de Europese Commissie te verzoeken om de toelatingsprocedure van de genetisch gemodificeerde (ggo)-zetmeel aardappel EH92-527-1 te bevorderen.

De Landbouwraad heeft in februari 2008 gestemd over het besluit voor de markttoelating van deze ggo-aardappel. Daarbij werd geen gekwalificeerde meerderheid voor of tegen het besluit behaald. Bij de discussie over de risicobeoordeling ging veel aandacht uit naar de mogelijke gevolgen van het antibioticaresistentiegen dat de aardappel bevat. Minister Cramer heeft mede namens mij, de Tweede Kamer in april 2008 hierover geïnformeerd[1]. In mei 2008 heeft de Europese Commissie de Europese Voedselveiligheid Autoriteit (EFSA) verzocht om wetenschappelijke gegevens over effecten van het gebruik van deze antibioticaresistentiegenen nader te analyseren.

Nederland heeft in het voorjaar van 2009 bij de Europese Commissie geïnformeerd naar de stand van zaken van het EFSA-onderzoek en verzocht de besluitvorming over toelating van de aardappel te bespoedigen. De Commissie antwoordde dat ze de besluitvorming over de toelating zal voorbereiden, zodra de analyse van de EFSA beschikbaar is.

Op 11 juni 2009 heeft de EFSA zijn wetenschappelijke opinie gepubliceerd over het gebruik van antibioticaresistentiegenen als merkergenen in genetisch gemodificeerde planten (zie bijgevoegde samenvatting). De EFSA stelt in deze opinie dat bij de nadere analyse geen nieuwe wetenschappelijke gegevens aan het licht zijn gekomen, die aanleiding zouden kunnen geven om de vorige positieve risicobeoordeling van de ggo-aardappel te wijzigen.

[1] Kamerstukken vergaderjaar 2007-2008, 27428, nr. 104

Ik ga er van uit dat de Europese Commissie op basis van deze en eerdere opinies van de EFSA over de ggo-aardappel en antibioticaresistentiegenen, spoedig een besluit zal voorbereiden over de markttoelating van de aardappel.

DE MINISTER VAN LANDBOUW, NATUUR EN VOEDSELKWALITEIT,

G. Verburg

Directie Voedselkwaliteit en Diergezondheid
Cluster Voedselveiligheid

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STATEMENT OF EFSA

EFSA-Q-2009-00589 and EFSA-Q-2009-00593

Consolidated presentation of the joint Scientific Opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" and the Scientific Opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants"[1]

Prepared by GMO and BIOHAZ Units

EUROPEAN FOOD SAFETY AUTHORITY (EFSA), PARMA, ITALY

SUMMARY

The following summary provides a consolidated overview of the joint scientific opinion of the GMO and BIOHAZ Panels on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" adopted on March 26, 2009 and the scientific opinion of the GMO Panel on "Consequences of the Opinion on the Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants on Previous EFSA Assessments of Individual GM Plants" adopted on March 25, 2009.

Following a request from the European Commission to the European Food Safety Authority (EFSA) the Panel on Genetically Modified Organisms (GMO) and the Panel on Biological Hazards (BIOHAZ) were asked to deliver a joint scientific opinion on the use of antibiotic resistance genes as marker genes in genetically modified (GM) plants. This opinion should take account of the previous opinion and the statement of the GMO Panel on the use of antibiotic resistance marker genes in GM plants intended or already authorised to be placed on the market and their possible uses as food and feed, for import and processing and for cultivation. It was asked whether the Opinion could explain the rationale leading to the conclusion of whether the use of each particular antibiotic resistance marker gene is likely or not to have adverse effects on human health and the environment and outline the reasoning

[1] On a request from European Commission, DG SANCO, Mandate No EFSA-M-2008-0411; issued on 14 May 2008.

leading to each conclusion. The opinion should also serve as a basis for the case-by-case safety assessment of each GM plant and its processed products.

The antibiotic resistance traits as present in GM plants and/or their derived products are evaluated on a case-by-case basis with respect to their safety for humans, animals and the environment by the GMO Panel according to the scientific principles expressed by the Directive 2001/18/EC of the European Parliament and the Council (EC, 2001) and detailed by the regularly updated guidance documents of EFSA (EFSA, 2006). The evaluation is based on molecular, biochemical, toxicological and environmental evidence.

The joint opinion of the GMO and BIOHAZ Panels (Annex 1) focuses on the two antibiotic resistance marker genes that are present in GM plants for which an application has been submitted to EFSA. One is functional in the plant (*aph(3')*-IIa = *npt*II, kanamycin/neomycin resistance); the other gene (*ant-(3'')*-Ia = *aad*A; streptomycin/spectinomycin resistance) is not expressed in the GM plants as the expression is regulated by a bacterial promoter not active in plants. The latter gene is used at the initial steps to develop the genetic constructs before introduction to the plant. An overview of relevant scientific literature is given and a qualitative risk assessment is provided. Whilst a detailed evaluation of *aph(3')*-IIa and *ant-(3'')*-Ia genes is included in the appendices, the opinion itself specifically addresses the indirect hazards.

From all the evidence gathered, the two Panels drew the following conclusions:

The transfer of antibiotic resistance marker genes from GM plants to bacteria has not been shown to occur either in natural conditions or in the laboratory in the absence of sequence identity in the recipient bacterial cell. Sequence identity is necessary to allow homologous recombination between the transformed DNA in the plant and bacterial DNA.

DNA transfer from GM plants to bacteria, if occurring, is considered to be of low frequency compared with gene transfer between bacteria.

Recent metagenomic analyses of total bacterial populations (including non-cultivable bacteria) have demonstrated that resistance determinants of kanamycin, neomycin and streptomycin are present in all environments investigated. Such resistance genes may be selected from this environmental reservoir and disseminated among bacteria.

The antibiotic resistance marker genes, *aph(3')*-IIa (*npt*II) and *ant(3'')*-Ia (*aad*A), in GM plants are of bacterial origin. These antibiotic resistance genes occur at different frequencies in different species, isolates and different environments, in naturally occurring bacteria. The spatio-temporal relationship between the prevalence of antibiotic resistance and selection pressure is not fully understood.

The presence of antibiotics and antibiotic usage in different environments are key factors in driving the selection and dissemination of antibiotic resistance genes.

Kanamycin and neomycin are both categorized by the WHO Expert Group on Critically Important Antimicrobials for Human Health as 'Highly Important Antimicrobial'. Kanamycin is used as a second-line drug for the treatment of infections with multiple drug-resistant tuberculosis (MTB). The increasing occurrence worldwide of "extensively drug-resistant" (XTB) isolates of MTB with resistance to second-line antibiotics such as kanamycin is a cause for global concern. The *npt*II gene has not been implicated in such resistance. The above WHO group has also categorised streptomycin as a 'Critically Important Antimicrobial', and spectinomycin as a 'Highly Important Antimicrobial'.

There are limitations related among others to sampling, detection, challenges in estimating exposure levels and the inability to assign transferable resistance genes to a defined source. The importance of taking these and other uncertainties described in this Opinion into account requires to be stressed.

Notwithstanding these uncertainties, the current state of knowledge indicates that adverse effects on human health and the environment resulting from the transfer of these two antibiotic resistance genes from GM plants to bacteria, associated with use of GM plants, are unlikely.

Two members of the BIOHAZ Panel expressed minority opinions on this last conclusion. Full details of the proposal for amendment of the mentioned conclusion are provided in Appendix D of Annex 1.

In addition, the European Commission requested EFSA to indicate the possible consequences of this new opinion on the previous EFSA assessments of individual GM plants containing antibiotic resistance marker genes. This aspect is addressed in the scientific opinion of the GMO Panel (Annex 2).

The GMO Panel has issued previously scientific opinions about the safety of two GM plant events that contain the *aph(3')*-IIa gene (*npt*II), i.e. maize MON 863 and hybrids and starch potato EH92-527-1. In the light of the new EFSA scientific opinion "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants", the GMO Panel is of the opinion that its previous assessments on GMOs containing this antibiotic resistance marker gene are in line with the risk assessment strategy described in the above opinion, and that no new scientific evidence has become available that would prompt the Panel to change its previous opinions.

Following adoption of these opinions by the respective Panels, EFSA consulted the Chairs of the GMO and BIOHAZ Panels as to whether the completion of the mandate would require a clarification of issues raised in the minority opinions of the joint scientific opinion (Letter addressed to the Chairs of the GMO and BIOHAZ Panels and to the Chair of the Joint Working Group - Annex 3). The Chairs responded by confirming that the scientific issues related to the minority opinions have already been extensively considered during the preparation of the joint scientific opinion and the formulation of the conclusions therein and thus, from a scientific perspective, further clarification of the joint scientific opinion is not required, nor is further scientific work needed at this time (Annex 4).

Key words: Directive 2001/18/EC, Regulation 1829/2003, GMOs, GM plants, antibiotics, antibiotic resistance marker genes, safety, food safety, human health, environment, horizontal gene transfer, *npt*II, *aad*A.