Minister for Food, Agriculture and Fisheries

Copenhagen, 14. march 2008
No.: 11371

Dear Commissioner Vassiliou and Commissioner Dimas,

In our positions as Danish Ministers of Food, Agriculture and Fisheries and of Environment respectively, we kindly ask the Commission to consider the following issue related to the risk assessment carried out in the process of GMO-approvals.

Antibiotic resistance is a matter of great concern to the Danish population, as well as to members of the Danish Parliament. Recently, these concerns have given rise to questions from Parliament members in connection with the Council negotiations of four Commission proposals to grant authorisation under Regulation (EC) 1829/2003 for the placing on the market of genetically modified organisms (GMOs), which contain the antibiotic resistance marker (ARM) gene *nptII*. These questions relate to concerns about a potential spreading of ARM genes from a GMO to bacteria in the environment and in the human intestine, and the risk of an increased amount of bacteria that are resistant to antibiotics used in the medical treatment of humans or animals. Danish Parliament members have questioned the validity of the scientific assessment of the risks involved.

As responsible Ministers, we take the above concerns seriously.

According to the European legislation on GMOs, a decision to authorise the deliberate release or the placing on the market of GMOs should be based on a scientific assessment of all potential risks involved in relation to human and animal health and the environment. This risk assessment is carried out by the European Food Safety Authority (EFSA) and by Member State experts.

With respect to the use of the *nptII*-gene as selective marker in GM plants (and derived food and feed) EFSA has concluded in an opinion of 2004 (the 2004-opinion) that this ARM does not pose a risk to human or animal health or to the environment. Danish experts agree with this conclusion.

However, the Danish experts are of the opinion that there is an inconsistency between the 2004-opinion and a recent EFSA-opinion, dated March 2007 (the "2007-opinion"), with regard to the categorisation of the *nptII*-gene according to the criteria laid down in the 2004-opinion as well as the conclusion and recommendation on the use of ARM genes. It is this inconsistency that has dominated the recent discussions in the Danish Parliament about the risks associated with ARM genes.

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In its 2004-opinion, the EFSA GMO-panel evaluated the potential risks associated with specific ARM-genes. The Panel considered that the likelihood of a horizontal gene transfer from GM-plants to other organisms is generally very low for all ARM-genes considered. The Panel furthermore stated that, if transfer of an ARM-gene from a GM-plant to a microbe should occur at all, the risk associated with this rare event should be viewed against 1) the natural presence of ARM-genes in soil, plant, water and enteric bacteria and 2) the therapeutic importance of the relevant antibiotics. Based on these two criteria, the GMO-panel in their 2004-opinion identified three groups, which the different ARM-genes were assigned to.

In the 2004-opinion, EFSA assigned the *nptII*-gene to group I, which contains genes that a) are already widely distributed in soil and enteric bacteria and b) confer resistance to antibiotics, which have no or only minor therapeutic relevance in human and veterinary medicine. On this basis, EFSA states that it sees no rationale for restricting or prohibiting the use of the genes in this group in GM plants.

Group II, as identified by EFSA, contains antibiotic resistance genes, which (a) are widely distributed in microorganisms in the environment and (b) confer resistance to antibiotics, which are used for therapy in defined areas of human and veterinary medicine. EFSA recommends that the genes in this group should be restricted to field trial purposes and should not be present in GM plants to be placed on the market.

In an opinion dated 22 February 2007, the European Medicines Agency (EMEA) indicates, that the amino glycosides, which the *nptII*-gene confers resistance to, may become increasingly important, and cannot be classified as having no or only minor therapeutic relevance in human and veterinary medicine.

Responding to EMEA's opinion, in its 2007-opinion EFSA reiterates the earlier conclusion (EFSA, 2004) that the use of the *nptII*-gene as selective marker in GM plants (and derived food and feed) does not pose a risk to human or animal health or to the environment. EFSA thus agrees with EMEA that it is important to preserve the therapeutic potential of the antibiotics involved, where relevant. However, EFSA finds that the therapeutic potential of the antibiotics involved is not at stake, considering the very small likelihood of occurrence of gene transfer, as well as the predominance of resistant bacteria in the natural environment. In other words, EFSA does not consider the criteria of *therapeutic relevance* of importance for the risk-assessment of the *nptII* gene.

As a consequence of EFSA's 2007-opinion, the *nptII* gene can no longer be assigned to group I as defined by EFSA in the 2004 opinion, because the criteria of therapeutic relevance of the antibiotics involved is not fulfilled. In line with EFSA's own criteria, the gene should rather be categorised in

group II. This categorisation, however, would imply that the gene should not be allowed in products for marketing. This is inconsistent with EFSA's own conclusion, that the nptII gene does not pose a risk.

EFSA does not in its 2007-opinion reconsider the criteria identified in its 2004-opinion for the categorisation of ARM genes, nor does it revise the recommendations for the use of ARM genes.

As stated above, Danish experts agree with EFSA's conclusion, that the *nptII* gene does not pose a risk. However, the above described inconsistency creates uncertainty about the results of EFSA's risk analysis.

In our view, the above mentioned discrepancies present a serious difficulty for risk administrators, especially in relation to the approval of GMOs with ARM-genes, and the phasing-out of ARM-genes according to Directive 2001/18. Due to the political sensitivity of GMOs, this uncertainty also influences the political debate regarding the approval of GMOs with ARM-genes under Regulation (EC) 1829/2003.

Therefore, we kindly ask the Commission to clarify this issue, preferably by asking EFSA to explain in more detail the rationale behind their conclusion in the 2007-opinion, as well as the impact of the latter opinion for the classification of and the recommendations for the use of ARM genes in the 2004-opinion and to consider the need to revise the classification defined by EFSA in the 2004 opinion.

Yours sincerely,

Eva Kjer Hansen / Troels Lund Poulsen

Minister of Food, Agriculture and Fisheries Minister of Environment