

24 April 2008

## Background briefing on BASF GM potato

### I. Inconsistencies regarding antibiotic resistance marker genes (ARMGs) – a chronology of events

The BASF potato contains the antibiotic resistance marker gene *nptII*, which confers resistance to two families of antibiotics: kanamycin and neomycin (according to EFSA).

**2001:** EU law (Dir. 2001/18/EC) states that any antibiotic resistance marker genes (ARMGs) which may have adverse effects on human health and the environment should be phased out by December 2004.<sup>1</sup>

**2004 April:** the European Food Safety Authority (EFSA) classifies 'marker' genes in three categories, according to the clinical importance of the antibiotics concerned<sup>2</sup>:

**Group 1** – marker genes conferring resistance to antibiotics "*which have no or only minor therapeutic relevance in human medicine*". These genes can be used in GM plants.

**Group 2** – marker genes conferring resistance to antibiotics "*used in defined areas of human and veterinary medicine*". These genes should be used only in field trials for experimental purposes.

**Group 3** – marker genes conferring resistance to antibiotics "*highly relevant for human therapy*". These genes should be banned "*irrespective of considerations about the realistic value of the threat*".

EFSA includes the *nptII* gene into Group 1, considering kanamycin and neomycin as antibiotics with "*no or only minor therapeutic relevance*".

**2005 February 15:** the World Health Organisation (WHO) classifies kanamycin and neomycin as "*critically important*" antibacterials.<sup>3</sup>

**2005 February 28:** BASF submits an application to place its GM potato on the market for food and feed uses.

**2005 December:** EFSA publishes a positive opinion on the authorisation of the BASF potato.<sup>4</sup>

**2006 December:** Greenpeace brings the WHO report to the Commission's attention.

**2007 February:** Following a request from the Commission to look into the matter, the European Medicines Agency (EMA) confirms the WHO position, stating that kanamycin and neomycin "*cannot be classified as of no or only minor therapeutic relevance*".<sup>5</sup>

**2007 March:** EFSA acknowledges its mistake in judging the relevance of kanamycin and neomycin: "*The GMO panel agrees with the EMA that the preservation of the therapeutic potential of [kanamycin and neomycin] ... is important*".

<sup>1</sup> Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms, Article 4(2) (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:106:0001:0038:EN:PDF>).

<sup>2</sup> Opinion of the Scientific Panel on Genetically Modified Organisms on the use of antibiotic resistance genes as marker genes in genetically modified plants (Question N EFSA-Q-2003-109). See page 11. The EFSA Journal (2004) 48, 1-18 ([http://www.efsa.europa.eu/EFSA/Scientific\\_Opinion/opinion\\_gmo\\_05\\_en1.2.pdf](http://www.efsa.europa.eu/EFSA/Scientific_Opinion/opinion_gmo_05_en1.2.pdf)).

<sup>3</sup> World Health Organisation, Critically Important Antibacterial Agents for Human Medicine for Risk Management Strategies of Non-Human Use. Report of a WHO working group consultation, 15-18 February 2005, Canberra, Australia ([http://www.who.int/foodborne\\_disease/resistance/amr\\_feb2005.pdf](http://www.who.int/foodborne_disease/resistance/amr_feb2005.pdf)).

<sup>4</sup> Opinion of the Scientific Panel on Genetically Modified Organisms on an application for the placing on the market of genetically modified potato EH92-527-1 with altered starch composition, for production of starch and food/feed uses, under Regulation (EC) No 1829/2003 from BASF Plant Science ([http://www.gmo-compass.org/pdf/regulation/potato/EH92-527\\_potato\\_assessment\\_EFSA\\_1829.pdf](http://www.gmo-compass.org/pdf/regulation/potato/EH92-527_potato_assessment_EFSA_1829.pdf)).

<sup>5</sup> European Medicines Agency (EMA) - Committee for medicinal products for veterinary use and Committee for medicinal products for human use, Presence of the antibiotic resistance marker gene *nptII* in GM plants for food and feed uses. EMA/CVMP/56937/2007. 22 February 2007 (<http://www.emea.europa.eu/pdfs/human/opiniongen/5693707en.pdf>).

However, EFSA fails to draw the obvious conclusions. On the basis of the WHO and EMEA scientific opinions and given the classification adopted by EFSA in 2004, the *nptII* gene must be moved into Group 3. GM plants cannot contain this gene (since December 2004).

Therefore, EFSA has disregarded:

1. the Commission request "*to indicate the possible consequences of the EMEA's conclusions on the safety assessment of the nptII gene*" (EFSA statement 13 April 2007),
2. the opinions of the WHO and EMEA, as well as
3. its own opinion from 2004.

**The Commission proposal to authorise the BASF potato is therefore based upon an opinion which is fundamentally flawed.**

## II. Other concerns raised by EMEA not addressed by EFSA

In March 2007 EFSA also failed to address two other crucial concerns expressed by EMEA.

1. EMEA stated: "*Occurrence of resistance to kanamycin and neomycin varies substantially between countries and bacterial species*" (EMEA opinion page 4, n.5). The variability of natural resistance to kanamycin and neomycin seriously challenges EFSA's generic statement that "*there is widespread presence of the nptII gene in bacterial populations*" and that therefore the use of *nptII* does not pose risks.
2. EMEA assumes that the *nptII* gene "*confers resistance to kanamycin, neomycin ... and not to gentamicin, otherwise normally expected. This [assumption] is crucial*" (EMEA opinion page 3, n.3). EMEA also highlights that EFSA bases this assumption only on two studies from 1993 and 1994 and that no reference to these studies could be located, concluding that it "*cannot therefore assess the scientific basis for this point, nor the independence of the authors*"! If the *nptII* gene also affects gentamicin, this would further confirm the classification of *nptII* in Group 3. Unfortunately EFSA failed to address this concern.

## III. Unfounded arguments used by EFSA

In 2007 EFSA recognised that the antibiotics concerned were relevant, which in itself, and according to EFSA's own classification, justifies a ban of the potato marker gene.

But EFSA maintained its positive opinion on the basis of two arguments:

- 1) the frequency of horizontal gene transfer from GM plants to other organisms is very low,
- 2) the *nptII* gene is already widespread in the environment.

But according to EFSA these are characteristics common to all ARMGs, of all three groups.

*"1. The frequency of horizontal gene transfer from GM plants to other organisms is very low for all three groups of ARMGs considered.*

*2. For all of the antibiotics and resistances considered, it has been shown or is extremely likely that there is a considerable extant pool of resistance genes already present in the microbiota in the environment."*

(EFSA 2004 conclusions)

**The only crucial factor is the relevance of the antibiotics affected**, which makes these arguments invalid. Even if we ignore the strength of this legal and scientific reality, EFSA's arguments would imply that all GM products containing marker genes should be authorised, since the argumentation applies to all ARMGs. This would have the added effect of undermining EFSA's own antibiotic categorisation.