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To the minister of
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Dr Jacqueline Cramer
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DATE 31 January 2008
REFERENCE CGM/080131-04
SUBJECT Response by COGEM to the French Opinion on MON810

Dear Mrs Cramer,

In response to a request for advice on the recently published report by the French *Comité de préfiguration d'une haute autorité sur les organismes génétiquement modifiés* titled 'Projet d'avis sur la dissemination du MON810 sur le territoire français', COGEM is pleased to advise you as follows.

Summary:
The recently published report by the French *Comité de préfiguration d'une haute autorité sur les organismes génétiquement modifiés* concludes that new facts about the genetically modified maize line MON810 raise questions about the consequences for humans and the environment of using MON810. COGEM was asked whether the French report gives cause to revise its opinion on MON810.
MON810 is a genetically modified maize line which expresses the *cry1Ab* gene which confers resistance to the European corn borer and other insects. MON810 has been authorised for import and cultivation in Europe since 1998 and commercial cultivation of this maize line in Europe started in 2003.
Since the introduction of MON810 numerous publications have appeared on research into the environmental safety of this maize line. None of these publications indicates that MON810 poses a risk to humans and the environment. In addition, publications on the possible effects of the Cry1Ab toxin do not show that this toxin poses a risk to humans and the environment. Monitoring reports on the cultivation of MON810 or other maize lines that produce the Cry1Ab toxin do not prove that the cultivation of these crops will lead to damaging effects.
Even in the light of the French report, COGEM considers that any risks associated with the cultivation of MON810 are negligible. COGEM is therefore of the opinion that there is no reason to rescind the authorisation of MON810.

The grounds on which COGEM has reached its conclusions and the resulting advice are set out in the enclosed report.

Yours sincerely,

Professor Bastiaan C.J. Zoeteman

Chairman of COGEM

c.c. Mr. A.B. Holtkamp
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Response by COGEM to the French report titled 'Projet d'avis sur la dissemination du MON810 sur le territoire français'

COGEM advice CGM/080131-04

1. Introduction

In January 2008 the *Comité de préfiguration d'une haute autorité sur les organismes génétiquement modifiés* issued an Opinion on the genetically modified maize line MON810 (1). The Comité was established in December 2007 to reconsider the risks and benefits of MON810 to humans and the environment. In its Opinion the Comité states that new facts on MON810 raise questions about the consequences of the use of MON810 for humans, the environment and the economy.

In the light of the report by the Comité, COGEM was asked whether the Comité's findings give reason to suspect that MON810 could pose risks to humans and the environment (see Annex). Given the limited time available, COGEM has prepared a brief response to the French report. COGEM plans to produce a more extensive response at a later date. This will provide a broader view of the problem and examine in more depth the literature that is not mentioned in the French report, but which may be relevant.

2. Background information on maize line MON810

MON810 is a genetically modified maize line which is resistant to the European corn borer. In 1996 COGEM gave a positive recommendation on the market authorisation of this line (2). MON810 was authorised by the United States in 1996 and has been approved for import and cultivation in Europe since 1998. MON810 was first commercially cultivated in Europe in 2003. In 2006 this maize line was cultivated in six EU countries (Spain, France, Czech Republic, Germany, Portugal and Slovakia). The largest area planted with MON810 (50,000 hectares) was in Spain (3).

The *cry1Ab* gene in MON810, taken from *Bacillus thuringiensis* subs. *kurstaki*, is expressed constitutively and codes for a δ-endotoxin. δ-Endotoxins are better known as Bt-toxins. The Cry1Ab Bt-toxin is specific for certain Lepidoptera, including the European corn borer. In insects susceptible to the Cry1Ab Bt-toxin, proteases in the midgut generate a toxic fragment from the endotoxin, which binds to specific receptors on the epithelium of the insect's midgut. This causes perforations in the membranes of the gut cells, enabling midgut bacteria to enter the body and infect the haemolymph system, resulting in death (4).

3. Maize

Maize (*Zea mays*) is cultivated around the world. It is fertilised mainly by cross-pollination, although a low percentage (5%) is fertilised by self-pollination. Maize is wind pollinated. Pollination by insects can occur, but is of minor importance. There are no wild relatives of maize in Europe and so outcrossing with wild relatives cannot take place (5). The pollen grains of maize are relatively large (90–125 μm) and heavy (0.25 μg), which means they can travel relatively short distances (6, 7). Experiments have shown that 90% of the pollen lands within five metres of the field boundary and 98% within 25 to 50 metres (8, 9). The wind direction has a strong influence on the dispersal pattern and the size and shape of the field also seems to have an influence on pollen dispersal.

Outcrossing with other cultivars can occur, but grains fertilised by cross-pollination are 'enclosed' within the maize cob and can only be dispersed by the action of humans (5). Maize grains have no dormancy period and so they can only survive under specific climatological conditions. As maize is susceptible to frost, under normal circumstances the grain cannot survive the Dutch winter. In addition, maize is highly susceptible to competition from weeds (10) and has lost its capacity to become established in the wild (5). Storage of maize plants is seldom observed in the Netherlands and no wild populations have ever been found. There is no reason to assume that the presence of the *cry1Ab* gene in MON810 increases the chances of this line becoming established in the wild.

4. Content of the French report and response by COGEM

In its report the French Comité states that since the authorisation of MON810 in Europe new scientific publications have appeared that raise questions about the consequences of the use of MON810 for humans, the environment and the economy. COGEM notes that the appearance of numerous publications on the safety aspects of MON810 does not automatically mean that there are misgivings about the risks of this maize line.

A meta-analysis of the possible effects on non-target organisms found no harmful effects in fields of MON810 (11). Neither have any adverse effects been reported from the monitoring of the cultivation of MON810 (3). In addition, data are available on the cultivation of the Bt176 maize line which, like MON810, expresses the *cry1Ab* gene. During a six-year field trial and monitoring of the cultivation of Bt176 no adverse effects were found on non-target organisms (12, 13).

COGEM also notes that crosses between MON810 and other maize lines, such as NK603xMON810 and MON863xMON810xNK603, have been assessed by various bodies. The European Food and Safety Authority (EFSA) has concluded that it is unlikely that negative impacts on humans and the environment are likely to occur as a result of importing and processing these hybrid lines (14, 15).

A number of topics covered in the French report are discussed in more detail below.

- **Degree of pollen dispersal**
  The French Comité concludes that outcrossing between GM maize and non-GM maize cannot be entirely prevented. COGEM is aware for some time of the data on wider dispersal of maize pollen resulting from certain weather conditions and environmental influences. COGEM points out that the dispersal of pollen from authorised maize lines does not pose any environmental risk and wider dispersal would not lead to a different judgement on MON810. There are no wild relatives of maize in Europe and so no outcrossing with wild relatives can take place (5). Maize cannot become established in the wild. Besides, even if MON810 should outcross with other cultivars, the fertilised grains would remain 'enclosed' within the maize cob. These grains can only be dispersed by the action of humans (5). Maize grains have no dormancy period and so under normal conditions will not be able to survive the Dutch winter.

  Outcrossing with other cultivars could lead to economic damage, though, if outcrossing leads to contamination of organic or conventional agricultural products. In an earlier report COGEM has addressed this problem of coexistence, including consideration of the data on dispersal of maize pollen resulting from certain weather conditions and environmental influences. At that time it concluded that with the use of buffer crops and isolation distances of 25 to 80 metres incrossing percentages can be achieved that are far lower than the EU threshold values (16).

- **Emergence of resistance**
  The Comité concludes that no new data are available on the emergence of resistance in the most important target organisms. The report does cite publications which seem to suggest that Cry1Ab resistant strains could arise among two secondary pests (belonging to the order Lepidoptera). COGEM is of the opinion that the emergence of resistant pests is an agricultural problem, but does not pose a risk to the environment. Such resistant organisms emerge not only through the use of pesticides but also the use of crops which have acquired resistance through conventional breeding methods.

- **Dispersal and persistence of Bt-toxin**

  The Comité writes that new data are available on the dispersal and persistence of Bt-toxin. Bt-toxin can find its way into the soil and bind to soil particles. Free Bt-toxin is broken down, but the rate at which this takes place depends on the composition of the soil, the temperature and the microflora present in the soil (17, 18). COGEM is of the opinion that any accumulation of Bt-toxin in the soil will only pose an environmental risk if it leads to adverse effects on soil organisms. Possible adverse effects are discussed in the following section.

- **Non-target organisms**

  The French Comité also refers to the possible effects of Bt-toxin on soil organisms. Various studies have been conducted on the possible effects of the Cry1Ab Bt-toxin on the soil flora and fauna. Although initially some effects were found on microbial populations, these appear to be caused by the higher lignin content of Cry1Ab Bt-maize (18). A study into the effects of Cry1Ab Bt-maize on soil organisms found, in comparison with a conventional maize line, a slight decline (12% to 9%) in the proportion of omnivore nematodes in the total nematode population. The variation that was found between Cry1Ab Bt-maize and a conventional maize variety is similar to the variation found between different soil types (19).

  The general picture that emerges from studies on the possible effects of Cry1Ab Bt-toxin on soil organisms is that no effects can be attributed to the presence of the Cry1Ab Bt-toxin (18). COGEM is of the opinion that any effects of MON810 on soil organisms will be totally outweighed by the natural variation arising from temperature differences, the type of crop cultivated or soil tillage methods.

  In addition, the Comité notes that adverse effects may occur on earthworms, woodlice, nematodes and the monarch butterfly, although the monarch butterfly is not present in Europe. COGEM points out that the studies mentioned (20, 21, 22, 23, 24) do not indicate any damaging effects on non-target organisms in the field. Moreover, a meta-analysis to investigate possible impacts of Bt-maize on non-target organisms in the field could not demonstrate any adverse impacts of MON810 (11).

  The Comité also looked at the exposure of insects at higher trophic levels. The referenced literature indicates that exposure of insects at higher trophic levels does not lead to any effects on these organisms. A possible exception is reported in a very recent study into the effects of Cry1Ab Bt-maize on a species of caddis fly (an aquatic

non-target organism) (20). Laboratory experiments conducted during this study revealed a negative effect on the growth of detritivore caddis flies (*Lepidostoma liba*) which were fed with plant material from Cry1Ab Bt-maize. It is not clear whether the amount of Cry1Ab plant material eaten was the same as the amount of material that would be eaten in a natural situation. Moreover, this caddis fly is not present in Europe (25). In addition, an effect was found on the survival of another caddis fly (*Helicopsyche borealis*). These effects were measured at pollen concentrations (2.75 g/m^2) two to three times as high as the measured concentrations in the field (20). This caddis fly is also not found in Europe (25).

The above-mentioned effects on caddis flies were observed under laboratory conditions, but there are no publications which report effects under natural conditions. The effects observed under laboratory conditions are described in a very recent publication. As a consequence, there are no other studies available which refute or verify these findings. Such studies are necessary in order to come to a final judgement. In an abstract presented at the congress of the North American Benthological Society the authors of the above-mentioned study report that no significant adverse effects were found in the field (26). These data have not yet been published in a scientific journal and are therefore not verifiable. On the basis of the currently available data, COGEM is of the opinion that there are as yet no reasons to assume that the risks are not negligible.

In addition to drawbacks implied by findings reported in the literature, the French Comité also mentions a number of problems that are not directly supported by scientific publications.

- One of these problems concerns the possible effects of MON810 on bees. Bees could ingest Cry1Ab Bt-toxin via pollen. However, the extent to which bees forage on maize is not known with any certainty and therefore we do not know how many maize pollens are consumed by bees. A study of possible effects of MON810 pollen or Cry1Ab Bt-toxin on bees found no effects on their survival or on the development of the hypopharyngeal glands (27). Hypopharyngeal glands are small glands that produce food for the larvae. Moreover, no Cry1Ab Bt-toxin was found in these glands in bees that were fed with MON810, and only traces of the MON810 Bt-toxin were found to be present in bees fed with sugar solution to which Cry1Ab Bt-toxin had been added (27). The authors conclude from this that larvae are less exposed to the Cry1Ab Bt-toxin than adult bees. Given the above, COGEM is of the opinion that there is no reason to expect that the Cry1Ab Bt-toxin will have any impact on bees.

- Further, the Comité states that 90-day feeding studies to investigate toxic effects on rats were insufficient to demonstrate any effects. In addition, they consider it desirable that epidemiological studies are conducted to investigate any impacts of MON810. COGEM points out that these studies were carried out according to the internationally recognised standard of the OECD. Questioning these studies and any subsequent adjustment of the findings would have wider significance than the safety assessment of GM crops because these studies are not only used in research into GM crops but also more generally in toxicity studies.

- In the context of biovigilance the Comité emphasised the importance of long-term studies into the effects of GM crops on flora, fauna, fungi and the ecosystem. COGEM agrees with this and notes that the legally required monitoring plan provides a guarantee that any impacts of MON810 will be noticed. The monitoring reports on the cultivation of MON810 that have been published give no reason to expect any risks to the environment.

5. Advice

The recently published report by the French *Comité de préfiguration d'une haute autorité sur les organismes génétiquement modifiés* mentions new facts and questions about MON810. The Comité concludes that these data raise questions about the consequences of the use of MON810 for humans and the environment.

COGEM is of the opinion that the literature mentioned in the report does not support the conclusion that scientific doubts can be cast on the accuracy of earlier considerations. Since the introduction of MON810 numerous publications have appeared on research into the environmental safety of this maize line. These publications contain no basis for the conclusion that MON810 poses a risk to humans and the environment. Neither do publications on the effects of the Cry1Ab Bt-toxin, which is produced by MON810, provide any indication that this toxin poses a risk. Equally, monitoring reports on the cultivation of MON810 or other maize lines that produce the Cry1Ab Bt-toxin do not indicate that the cultivation of these crops will lead to damaging effects.

Even in the light of the French report, COGEM considers that any risks associated with the cultivation of MON810 are negligible. COGEM is therefore of the opinion that there is no reason to suspend authorisation of MON810.