NOTIFICATION C/NL/0010

Summary of the evaluation carried out by the Netherlands Competent Authority.

1. THE NOTIFICATION

The notification, submitted by Pioneer Hi-Bred International Inc., Des Moines, U.S.A, and Mycogen Seeds, c/o Dow AgroSciences LLC, Indianapolis, U.S.A., concerns the placing on the market of seeds derived from genetically modified maize (*Zea mays* L.) line 1507 in accordance with Directive 2001/18/EC. The maize line 1507 is modified with the genes *pat* and *cry1F*, resulting in tolerance of the genetically modified maize to the herbicide glufosinate-ammonium and in tolerance to specific insect pests.
This notification only concerns import, use as feed and processing for food and feed purposes of line 1507. In this document, line 1507 will be used to refer to the transformant 1507 itself and to progeny derived from line 1507 by conventional breeding methods with non-genetically modified maize.

In 2001 another notification was submitted in Spain (C/ES/01/01) concerning placing on the market of line 1507 in accordance with Directive 2001/18/EC. This notification also concerns cultivation of maize, and is still under consideration by the Spanish competent authorities.

2. SCOPE OF THE NOTIFICATION

The notification covers the import, use as feed and processing for food and feed purposes, of 1507 maize and from any progeny derived from line 1507 by conventional breeding methods with non-genetically modified maize. This notification does not include cultivation of line 1507.

3. DEFINITIONS

In this document the following terms are used:

a. the Netherlands Competent Authority: the Minister of Housing, Spatial Planning and the Environment, in agreement with the Minister of Agriculture, Nature Management and Fisheries;
b. the GMO Decree: the Genetically Modified Organisms Decree pursuant to the Chemical Substances Act (Bulletin of Acts and Decrees 16 August 1993, 435);
c. the COGEM: the Committee on Genetic Modification, as established by the Environmental Management Act;
d. the Directive: the Council Directive of the European Union of 12 March 2001 on the deliberate release of genetically modified organisms to the environment (nr. 2001/18/EC);
e. the RIKILT-DLO: the State Institute for Quality Control of Agricultural Products.

4. PRECAUTIONARY PRINCIPLE

In accordance with the international principles for protection of the environment and the human health, the precautionary principle will be applied to the assessment of activities with genetically modified organisms. The precautionary principle in relation to the protection of the environment is described in 1992, in the 'Declaration of Rio de Janeiro on the Environment and Development':

'In order to protect the environment, the precautionary approach should be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation'

This means that in the risk-analysis and risk-assessment it should be explicitly considered whether the activities with the genetically modified organisms could lead to serious or irreversible damage, which is related to the genetic modification, of the human health and the environment.

5. LIST OF DOCUMENTS

The documents submitted by Pioneer Hi-bred that have been evaluated by the Netherlands Competent Authority are the following:
-Notification, titled: "Import of 1507", dated November 23, 2000;
-Additional information on aspects of the environment and of human health and feed safety dated February 14 (2001), October 16 (2001), January 30 (2002), November 21 (2002), March 24, (2003), May 28 (2003).

6. SCOPE OF THE EVALUATION

Within the context of the directive 2001/18/EC the scope of the evaluation is focussed on three main areas:
- aspects of the environment
- aspects of feed safety
- aspects of human health.

These three areas will be further discussed under point 8. Aspects of risk analysis and evaluation.

The evaluation of the use as food is not within the scope of the 2001/18/EC, but falls within the scope of the Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. The use of the herbicide and aspects related to the use of the herbicide are covered by the Council Directive 91/414/EEC of 15 July 1991 concerning the placing on the market of plant protection products.

7. PROCEDURE

In the Netherlands, the production, transport, use, possession, supply to third parties and disposal of genetically modified organisms are subject to the Environmental Management Act and the GMO Decree. These regulations do not apply in case products are placed on the market in accordance with Directive 2001/18/EC. Under part C of the Directive 2001/18/EC the following procedure is followed in the Netherlands.

Upon receipt of a notification for placing on the market and after acknowledgement of its completeness, copies are sent to:

- the COGEM for scientific advice on human health and environment related aspects;
- the RIKILT-DLO for its opinion on feed safety and related aspects;
- other relevant ministries, amongst which the Ministry of Agriculture, Nature and Fisheries.

At any point the procedure can be suspended to request additional information from the applicant. The procedure will only be restarted when the additional information is received by the competent authority within a given period of time and is reviewed as being sufficient.
Upon receipt of a notification, the Summary Notification Information Format is forwarded to the European Commission, who makes it publicly available. During 30 days the public can make comments.
Within 90 days upon receipt of the notification, an evaluation is made in which the following is taken into consideration: the notification, the advice from the COGEM, the opinion of the RIKILT-DLO, when applicable, and comments from other relevant parties. Data from comparable notifications in other countries are also considered.

On the basis of this evaluation, a final opinion (positive or negative) is given that is sent to the European Commission, together with the dossier. From there it will be distributed to all other European Member States for consultation. In case of a positive opinion, Member States have 60 days to evaluate the notification and to raise objections, make comments or request additional information, when thought necessary. If there are no objections or reactions, the rapporteur Member State gives consent in writing and the product can be placed on the EU market. If objections are raised or reactions are given, a period of 45 days will follow in which the Member States and the European Commission can discuss any problems and come to an agreement. If after these 45 days objections remain, a decision will be taken in accordance with the Committee procedure of article 30 of the Directive (= art. 30 procedure): the Commission will draft a Proposal for Commission Decision that will be submitted to the Regulatory Committee of the Member States and can be adopted by qualified majority. The advice of the Scientific Committee of Plants (SCP) of Directorate General Consumer Health Protection (former DG XXIV) is asked before drafting a Proposal for Commission Decision. If a qualified majority is reached by the Committee, the Proposal shall be adopted. If no qualified majority has been obtained, the Commission Proposal is forwarded to the Council of Ministers (of the Environment). The Council can adopt or reject the proposal by qualified majority. If the Council does not deliver an opinion within the given time frame, the Commission proposal shall be adopted.
Based on the outcome of the process described above, the Commission proposal will be either adopted or rejected. This means that the final decision on the notification can be either positive or negative. This official Decision of the Commission will be published in the Official Journal. The rapporteur Member State will act according to the Commission Decision and shall give the consent for marketing or shall reject the consent.

8. ASPECTS OF THE RISK ANALYSIS AND EVALUATION

According to article 4.3 of the Directive 2001/18/EC, a consent for placing on the market of products, which contain or consist of genetically modified organisms, can only be approved when it is ensured that the potential adverse effects on human health and the environment are accurately assessed on a case-by-case basis. For this purpose, a risk analysis and evaluation is carried out in accordance with Annex II

This risk analysis is in general based on an assessment of the characteristics of the genetically modified organism and of its intended applications. In this respect, the following general questions are important:

- Are there reasons to assume that the genetically modified organisms or its progeny, due to the genetic modification, will become hazardous to human health or the environment?
- Could the genetic material inserted into the genetically modified organisms be transferred to other organisms, and are there reasons to assume that those organisms, as a result, will become hazardous to human health or the environment?

These questions can not be answered straightforward. For that reason, the risk-analysis is structured based on international scientific consensus. In the analysis the following specific aspects are taken into account:

1. the relevant characteristics of the host organism;
2. the inserted sequences and traits;
3. the characteristics of the genetic modified organisms itself, as far as known from experiments;
4. the use of the product and the effects of the use.

The analysis should clarify the nature of the possible unwanted effects on human health and the environment that can be expected as a consequence of the intended activities and give an indication of the way these effects can occur. It is not the intention, in line with the precautionary principle, to set up a merely theoretical reasoning, but to come to a reasonable substantiation if certain effects can occur. In the Netherlands the analysis and evaluation of possible effects of the activities takes into account, amongst others, the following aspects:

1. A determination of the scale of the potential effects. An important issue is the occurrence of outcrossing. If this is the case, it is considered whether spread of genetic material is limited to cultivated plants or that outcrossing can occur with related species. Another point of consideration concerned with the scale of the potential effects is the possibility that uptake of the inserted sequences by microorganisms can lead to effects on the human health or the environment.

2. The nature of the potential effects that may be related to the genetic modification. In considering potential effects related to the genetic modification, very diverse aspects are evaluated in the risk analysis and –assessment, like:

a. environment
- effects on (populations of the) same species;
- effects on (populations of) related species with which the genetically modified plants are able to cross;
- effects on (populations of) other organisms that will be exposed to the genetically modified organism, or wild relatives with which the genetically modified organism can cross;
- the ecological consequences of the above mentioned effects. Special attention is given on the one hand to effects on specific populations of microorganisms, insects, birds, etc., and on the other hand to the different ecosystem functions.

b. aspects of human health
- allergenicity;
- toxicity upon incidental consumption;

- the consequences of the spread of the inserted genetic material (for example sequences coding for antibiotic resistance, pathogenicity factors, toxins, etc.) for the human health or the consequences for the use of certain compounds for therapeutic purposes.

c. feed safety

- the safety of the target animal, taking into account the consequences of toxicity of the product as well as consequences resulting from a change in composition of the components of the product;
- the safety for human consumption of the products derived from animals fed with the genetically modified plants.

This list is not limitative. It will depend on the application of the genetically modified organism if other aspects are considered. In general only a subset of the above mentioned points of interest will be relevant in relation to the genetic modification and the intended use.

9. SCIENTIFIC ADVICE BY THE COGEM

Based on the notification of November 23rd (2001), the COGEM concluded that insufficient information was supplied by the applicant to make a proper assessment of the notification. Therefore, additional information was requested from the applicant on December 15th (2000) and March 19th (2001) on the molecular characterization of the genetically modified maize line and on possible allergenicity and toxicity of line 1507. On March 25th (2002) more information was requested on the equivalence of the microbial and plant produced *cry1F*, as the applicant has conducted several experiments with microbial produced *cry1F* instead of the plant-produced protein. Also, more detailed information was requested on the expression of the *pat* gene and the possible adverse effects resulting from expression of ORF3 and ORF4.
On January 15th, 2003 (CGM/030115-01), the COGEM gave its advice on this notification and the additional information. Based on an evaluation of the possible risks to human health and the environment, the COGEM concluded that no significant potentially negative effects were identified related to the proposed placing on the market of the product.

10. OPINION OF THE RIKILT-DLO

On March 13 (2001), November 29 (2001), February 27 (2002), January 14 (2003), and April 16 (2003) the RIKILT-DLO gave its opinion on the notification. Based on an evaluation of the complete dossier, the RIKILT-DLO concluded that there is no indication that the product would not be safe when used as animal feed. This conclusion was based on the opinion of the RIKILT-DLO that 1507 maize and hybrids derived from line 1507 are comparable to conventional maize with respect to compositional analysis of kernels. In addition, the conclusion was based on results given by the applicant concerning safety testing of the gene products, degradation in the digestive tract, and target animal feeding studies.

11. RISK ANALYSIS AND EVALUATION OF MAIZE LINE 1507

In the analysis of this notification the following specific aspects are taken into account:

- the relevant characteristics of the host organism;
- the inserted sequences and traits and their combination;
- the use of the product.

A. Characteristics of the host organism

The scientific name of the parental organism is *Zea mays* L., also known as maize or corn. Maize is a member of the family *Gramineae*. The species *Zea mays* was probably produced as a result of domestication of the wild species teosinte, *Zea mexicana*, about 8,000 years ago in Mexico. Since the European settlement of the Americas, maize has been continuously cultivated in Europe and the Americas, as well as other parts of the world. In the domestication of maize from teosinte, amongst others a nonshattering rachis (cob) in maize was obtained in comparison to a shattering cob in teosinte.

Maize is an annual, monocotyledonous plant and seeds are the only survival structures. Natural regeneration from vegetative tissue is not known to occur.

The maize culture cycle ranges from 9 to 48 weeks from seedling emergence to maturity. This divergence in maturity time allows maize to be grown over a wide range of climatic conditions. Self-pollination and cross-pollination are usually possible and frequencies of each are determined by physical proximity and other environmental influences on pollen transfer.

A maize plant is usually comprised of a single stem with broad, flat alternating leaves attached to the stem or stalk by overlapping sheaths. Maize has unisexual flowers. Male flowers develop on the top of the plant, comprising an organ known as a tassel. Female flowers typically develop clustered on ear shoots along the stem of the plant. Typically, one to three ear shoots develop per plant. Maize seed does not readily disperse in the environment, as the seed is large and the seed-bearing ear is enclosed by husk leaves.

Maize seeds do not have a dormancy phase, and seed germination will therefore take place soon after shedding in the autumn. Germinated seeds are susceptible to cold weather and fungal infestation. The species is biologically contained within Europe and for survival it depends on human intervention. There are no wild populations of maize known in Europe.

Maize has no sexually compatible wild relatives in Europe. *Zea mays* is able to hybridize with wild species of the genera *Tripsacum* or *Zea*; these species are limited in geographical area to Mexico and Guatemala. The dispersal of maize genetic material through hybridization is limited in Europe to other maize grown in culture.

B. The inserted sequences and traits

To obtain genetically modified maize line 1507, maize embryos were modified by particle acceleration with a gel-purified linear fragment of 6235 base pairs (PHI8999). The fragment was obtained from vector PHP8999 and contains the *cry1F* gene and the *pat* gene. The *cry1F* gene is regulated by the maize *ubiZM* 1(2) promoter and the ORF25PolyA terminator from *Agrobacterium tumefaciens.* The *pat* gene is regulated by the 35S CaMV promoter en 35S terminator from Cauliflower mosaic virus.
It was confirmed by Southern analysis that only one copy of the gene cassette containing the *cry1F* gene and the *pat* gene was present in line 1507.

In case an applicant demonstrates that the borders of an insert are intact, flanking regions are not considered relevant in connection to adverse effects on human health and the environment. The occurrence of plant DNA rearrangements or (de)activation of plant genes in flanking sequences resulting from the insertion of foreign DNA is not directly related to the genetic modification itself, but is inherent to the process of plant

breeding in general. However, in case borders of an insert are proven not to be intact, the occurrence of truncated genes at the border of the insert may give rise to the formation of chimaeric proteins which are the result of the genetic modification and that may have an adverse effect on human health and the environment. In that case additional information is requested on the specific flanking region in relation to identified ORF's and possible expression of these ORF's.
The 5' flanking side of the insert in line 1507 was demonstrated to contain a truncated part of the *cry1F* gene, and additional data were requested on this 5' flanking side. Sequencing data revealed three ORF's in the 5' flanking side: two ORF's corresponding to maize DNA and one ORF (ORF3) that consisted of part of the *cry1F* gene, the maize chloroplast *rpoC2* and the *UbiZM* promoter. ORF3 codes for a hypothetical protein of 250 amino acids. Based on the results supplied by the applicant it was concluded that expression of ORF3 was not detectable with the detection assays used. No homology was detected for ORF3 with known toxins or allergens. From these data it can be concluded that expression of ORF3 is below the limit of detection. Even if ORF3 is expressed at low levels, this will not result in adverse effects on the environment because of the lack of homology of the putative protein with known toxins or allergens.

According to the guidance document on the risk assessment of genetically modified plants and derived food and feed dated March 2003, which elaborates on the guidance notes under 2001/18/EC and which is made by the EU Joint Working Group on Novel Foods and GMOs, also the 3' flanking sequence of the insert was assessed on potential ORF's. No ORF's coding for putative proteins of larger than 100 amino acids have been identified.

It is known that fragments obtained by gel purification may still contain other sequences present in the digestion mixture that was applied to the gel; in this case it concerned sequences from the backbone of vector PHP8999. For this reason also sequences from this vector could be inserted in the plant during the transformation process. Therefore plant line 1507 was checked on the absence of vector backbone sequences of PHP8999. This backbone contains the *nptII* gene (resistance to kanamycin) as a selection marker. Sequences of the vector backbone, including the *nptII* gene, were proven to be absent.

From the experimental data supplied by the applicant it was concluded that the molecular characterization of line 1507 was sufficient to substantiate the above-mentioned presence of the *pat* en *cry1F* gene and absence of the vector backbone sequences. Furthermore it was concluded that ORF3, even if it is expressed at a low level, does not form a risk to human health and the environment because of its lack of homology with known toxins and allergens.

B.1 Herbicide resistance

The synthetic *pat* gene (adjusted to the codon use in plants) is derived *from Streptomyces viridochromogenes* and codes for the enzyme phosphinothricin-N-acetyltransferase, PAT. The *pat* gene is used in plants to confer tolerance to glufosinate ammonium herbicides, because its gene product PAT inactivates glufonisate ammonium. PAT is earlier assessed in genetically modified oilseed rape (C/UK/95/M5-1), and in maize (C/GB/96/M4-01 and C/FR/95/12-07).

B.1.2 Selective advantage

Maize is not considered to be a weed in Europe and volunteers are rare. Maize plants resistant to glufosinate ammonium can only have a selective advantage under conditions that the herbicide is applied. Herbicides such as glufosinate-ammonium. are applied on arable land and roadsides to manage weeds. However, glufosinate-ammonium is not persistent and therefore after treatment the duration of any selective action due to the glufosinate ammonium is limited. Herbicides as glufosinate-ammonium are in general not used in the wild flora.

Therefore, there are no reasons to assume that the herbicide resistance, based on the expression of the PAT gene product, will provide a selective advantage to maize.

B.1.3 Toxicity and allergenicity.
The activity of the *pat*-gene product PAT is highly specific for phosphinothricin as a substrate. PAT shows no activity with glutamate, of which phosphinothricin is an analogue, or other glutamate analogues. The PAT protein itself is heat and pH labile and is rapidly degraded upon exposure to mixtures of digestive tract enzymes. Thus, it is unlikely that this enzyme will give rise to toxic or allergenic effects upon incidental consumption or when present in feed for animals.

The PAT protein encoded by the *pat*-gene does not have any characteristics of an allergen or a toxin. The gene only shows homology to other genes encoding PAT proteins, and the PAT protein shows homology only to other PAT proteins. There is no significant homology on the DNA level to any other gene or protein sequences in the GenBank, a database that contains known toxins and allergens. Furthermore, on the protein level no immunologically significant sequence similarities between the PAT protein and known allergen sequences were found in public gene sequence databases.

The PAT protein that is coded by line 1507 is the same protein as the PAT protein in maize line T25, which is already admitted to the European market (C/FR/95/12-07). From the results of the toxicity studies for the T25-expressed PAT protein it was earlier concluded that there were no reasons to question the safety of maize lines expressing this protein. The applicant has not provided any additional toxicity studies on the PAT protein in line 1507.

There are no reasons to assume that the gene product itself, a catalytic protein, will have a toxic effect upon incidental consumption or when present in feed. Neither are there reasons to assume that the reaction and/or degradation products of the catalytic activity will have a toxic effect.

B.1.4 Herbicide use
The use of the herbicide and aspects related to the use of the herbicide is covered by the Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. Before glufosinate-ammonium herbicides are used in maize crops expressing the PAT protein, these herbicides will have to be registered for extension of the use.

B.2 Insect resistance
The *cryIF* gene is a synthetic version of the gene derived from *Bacillus thuringiensis* and introduced in line 1507 to provide a reduced susceptibility to infestation by plant pests such as the European corn borer, *Ostrinia nubilalis,* and *Sesamia spp.* Its expression product is characterized by the applicant for molecular weight, immunogenicity, amino

acid sequence, insecticidal activity, and presence of glycosylation. 1507 plants were shown to produce a CRYIF protein identical to the trypsin resistant (tryptic) core of the CRYIF protein produced in *Bacillus thuringiensis*.

B.2.1 Selective advantage

The expression of the *cryIF*-gene provides the maize plants with a selective advantage when the plant is under attack by insect species susceptible to CRY1F. Nevertheless insect pests are not the major element in the selective pressure (consisting of physical and biological components) on maize within Europe, as the survivability is mainly limited by the absence of a dormancy phase, the susceptibility to fungi and the susceptibility to cold climatic conditions. This position is substantiated by the fact that despite the fact that B.t. maize plants have been cultivated for many years, there are no reports either in literature or from companies which describe an increased fitness of maize plants expressing *Bacillus thuringiensis* (B.t.) proteins.

Therefore, there are no reasons to assume that the expression of the gene *cryIF* will provide a selective advantage to maize that influences the weediness.

B.2.2 Toxicity and allergenicity

Acute toxicity studies were performed with mice, in this study no toxic effects could be detected.

The CRYIF protein has been shown to be highly specific and is insecticidal to certain lepidopteran insects. It is common knowledge that the specificity of B.t.-toxins is directly attributable to the presence of receptors in the midgut of target insects. There are no receptors for the delta endotoxins of *Bacillus thuringiensis* subspecies on the surface of mammalian intestinal cells, therefore humans and other mammals are not susceptible to these insecticidal proteins.

In addition to the lack of receptors for *Bacillus thuringiensis* (B.t.) proteins in humans, the absence of adverse effects in humans is further supported by numerous reviews on the safety of B.t. proteins. There is over 30 years of commercial use of B.t. toxin preparations in organic farming without any report of allergenicity attributed to the B.t. insecticidal proteins, including occupational allergy associated with manufacture of *Bacillus thuringiensis* preparations. No significant homology of CRY1F to proteins other than B.t. endotoxins was found.

Data in the application show that the CRYIF protein itself is rapidly degraded upon exposure to mixtures of digestive tract enzymes, and protein is inactivated after heating at 75 ^{0}C. These data strongly indicate that the protein has no allergenic potential

Therefore, there are no reasons to assume that the gene product itself, an insecticidal protein, will have a toxic or allergenic effect on humans or animals upon incidental consumption or when present in feed.

B.2.3 The effects of the insecticidal protein on non-target insects

The effect of the CRY1F protein is tested by the applicant on a range of non-target organisms. No acute or toxic effects were observed in these assays.

From these considerations with respect to the introduction of the described sequences and traits, no reasons have emerged on the basis of which a consent to the proposed placing on the market should be withheld.

C. The use of the product

The product is intended to be used as animal feed and for processing for food, animal feed, and industrial purposes.
The primary use for maize grain is as animal feed. According to the application maize grain may also be wetmilled to produce starch, feed, syrup, oil, and dextrins. Maize can be dry milled to produce meal, flour, grits, oil and breakfast cereals. In addition, the distilling and fermentation industries in the United States produce ethyl and butyl alcohol's, acetone, and whisky from maize. Maize products enter many human foods including bakery and dairy products, beverages, and confections. Industrial uses include paper products, construction materials, textiles, metal castings, pharmaceuticals, ceramics, paints, explosives and many others.

Use as feed

Since 2002, the use of feed obtained from line 1507 is approved in Canada and Japan.

The use as feed has been evaluated by RIKILT-DLO and next to the above mentioned aspects the following aspects are considered:

- the type of feed derived from the product;
- the animals the feed is intended for;
- previous evaluations concerning the safety of line 1507 for use as feed or food in other countries;
- compositional analysis of line 1507;
- equivalence van line 1507 with non-modified maize;
- implications for safety of animal feed.

Target animal feeding studies performed by the applicant with the whole maize kernel commodity in chicken and dairy cattle indicate that maize is nutritionally equivalent to other, conventional, maize varieties.
The results of the compositional analysis of hybrids obtained from line 1507 and comparable non-genetically modified maize showed no significant differences, except for the CRY1F and the PAT protein. From these data is was concluded that line 1507 and its products made thereof would be safe for use in animal feed prepared according to common practice.

Use as food

The evaluation of the use as food falls within scope of the Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. The maize line 1507 is still under consideration for admission to the European market for use in human food under this regulation.
Line 1507 is already admitted for food in the United States (FDA), Japan and Canada.

Taking in to account the relevant characteristics of maize (cannot propagate itself, is not weedy and has no wild relatives in the EU), the inserted *cry1F* and *pat* gene, and the use of the imported product as animal feed and for processing, it can be concluded that:

- maize of line 1507 which is introduced into the environment as a result of spillage will not be able to propagate itself;
- the risk of import and processing of 1507 maize for human health and the environment is negligible.

12. HANDLING AND PACKAGING

In the risk assessment no potential adverse effects on human health and the environment could be identified in relation to the use of the imported product for feed and processing. Spillage of seeds will not lead to a stable population of maize plants. Outcrossing will not occur, since there are no sexual compatible wild relatives in Europe. For this reason, no specific conditions are necessary for handling and packaging of the 1507 maize.

13. LABELLING

Product information with regard to the import of bulk mixtures of maize grain will be provided by the applicant to those who buy, use or process maize line 1507, to indicate that genetic modification has been used in the development of 1507 maize and will be provided on a label and/or accompanying document. This information will include:

- the commercial name of the product, being 1507 maize with the unique identification code DAS-Ø15Ø7-1 and the statement that "this product contains genetically modified organisms";
- the name of the GMO;
- name en full address of the notifier;
- how to access the information in the publicly accessible part of the register meant in article 31, para 2 of 2001/18/EC;
- the use of the product, that will not be different from current uses of maize grain.

This product information is considered to be in accordance to Annex IV of the Directive 2001/18/EC.

14. MONITORING

Taking into account that the intented use of the placing on the market of this product is the import and processing, including feed use, the monitoring plan is based on the identification, surveillance and traceability of grain of maize line 1507, providing information to traders, processors and end-users in order to identify any adverse effects on the environment or human health. The applicant proposes to use existing networks for surveillance purposes, including networks in the agronomic environment, the non-agronomic environment and people and networks involved in human and livestock health. The applicant will report on the results of the surveillance, which will include feedback from the selected external networks and potential adverse effects and other relevant information that are reported via the Company network or toll-free telephone number.

15. DETECTION METHOD

The applicant has provided a detection method that is specific for event 1507, as is obligatory under the 2001/18/EC. The detection method is verified by the Netherlands and was proven to be adequate for detection and identification of line 1507 under laboratory conditions.

16. PUBLIC COMMENTS TO THE NOTIFICATION C/NL/00/10 AND REACTION OF THE NETHERLANDS COMPETENT AUTHORITY:

The notification C/NL/00/10 has been made public by the European Commission on the internet site of the Joint Research Centre (JRC) on February 14 (2003). During 30 days the public had the opportunity to comment on all aspects of the notification.
The Netherlands CA has summarized these comments on C/NL/00/10 and briefly addressed them.

There is no market for GMO's in Europe

There being a market for GMO's in Europe or not, is not relevant for the part C applications under directive 2001/18/EC. The legal framework under directive 2001/18/EC provides only for human health and environmental risks to be taken into account.

Admission of GMO's is in conflict with the precautionary approach

A conflict with the precautionary principle would arise, if in the light of scientific uncertainty, cost effective measures to prevent risks to human health and the environment, would not be taken. The precautionary principle in the consent of the Dutch Competent Authority is, amongst others, put into practise through (1) the notification of the 1507 maize, (2) a thorough risk analysis and (3) additional provisions in the consent.

Market approvals should not be given before the regulations on labeling/traceability and for food/feed are approved, or before the liability and co-existence issues are resolved

These regulations and issues do not affect the outcome of the risk assessment for import of maize line 1507. The legal framework of 2001/18/EC does not provide a possibility to postpone handling dossiers for market release of gmo's. Therefore there is no scientific reason nor a legal possibility for the above mentioned regulations to be approved, or the liability and co-existence issues to be resolved, before market approval of line 1507 can be granted under the 2001/18/EC.

No GMO's should be admitted that contain genes expressing resistance to antibiotics.

Maize line 1507 was demonstrated not to contain antibiotic resistance genes as a result of the genetic modification.

The monitoring plans for cultivation are not sufficient

Maize line 1507 will not be cultivated. The notification concerns with import, feed and processing, but excludes cultivation.

No feeding studies are undertaken

In dossier C/NL/00/10 several studies are included in which the feed safety of line 1507 maize is addressed.

Any insecticide is likely to be potential harmful to humans and animals

This specificity of Bt toxins is directly attributable to the presence of receptors in the mid gut of target insects. There are no receptors for the delta endotoxins of *Bacillus thuringiensis* subspecies on the surface of mammalian intestinal cells, therefore humans and other mammals are not susceptible to these insecticidal proteins.
Bt toxins are widely applied in agriculture as sprays, and no negative effects have been reported so far. As is mentioned in the specific comment, also CRY1F is applied as a spray by organic farmers.

There are no long term studies on the toxicity of plant/food/feed to any humans, livestock or non-target organisms for the GMO's applied for Further toxicological testing is necessary along the lines of those applied for pharmaceuticals

Maize will be mainly used for feed. The tests supplied in the dossier and the nature of

the proteins coded by the inserted genes do not indicate that maize line 1507, based on its genetic modification, is toxic to animals. The observation of possible unexpected effects on livestock is anticipated in the general surveillance plan that is part of the notification.

- **Beekeepers will be severely threatened by growing GM crops because the honey will not be GM-free and people can be allergic to the novel proteins that could end up in the honey.**

The market approval is not for cultivation of maize.

Cross pollination can occur between GM maize and non-GM maize

Cross-pollination between GM maize and non-GM maize is highly unlikely, because the scope of the notification does not include cultivation of maize. Furthermore, volunteers as a result of spillage, will hardly occur due to the fact that maize seeds do not have a dormancy phase; seed germination will therefore take place soon after shedding and in addition, germinated seeds are susceptible to cold weather and fungal infestation which leads to the death of those seeds.

Cultivation of Bt plants will lead to Bt-resistant pests, possibly with a higher fitness
Cultivation of herbicide resistant plants will lead to gene stacking of herbicide resistance traits.

The notification does not include cultivation of line 1507 maize.

17. ADVICE OF THE NETHERLANDS COMPETENT AUTHORITY FOR DIRECTIVE 2001/18/EC

Based on the notification, the appendixes and the above considerations, the Netherlands Competent Authority concludes that no reasons have emerged on the basis of which consent to the proposed placing on the market should be withheld.

The Netherlands Competent Authority therefore proposes to consent to the placing on the market of the product as described below, for which a notification has been submitted on November 23, 2000, registered under number C/NL/00/10 under explicit specification of:

a) The consent will be granted to Pioneer Hi-Bred International, Inc. and Mycogen Seeds, c/o Dow AgroSciences LLC and concerns the placing on the market under part C of 2001/18/EC of the product 1507 consisting of maize genetically modified with the *pat* and *cry1F* genes, thereby rendering it tolerant to certain insects and to glufosinate-ammonium herbicides, with the unique identification code DAS-Ø15Ø7-1 for the purpose of import, direct use as feed and for all processing purposes, of line 1507 and from any progeny derived from line 1507 by conventional breeding methods with non-genetically modified maize. This consent does exclude cultivation of line 1507.
b) Pioneer Hi-Bred and Mycogen Seeds are severally liable to observe the conditions which are directed to the consent holder of this consent in its entirety.
c) The consent will be valid for a period of 10 years after approval.
d) The company should give sufficient guarantees that the product information supplied to those who buy or use the product will be passed on during all transport and handling of line 1507.

e) The consent holder is required to supply reference material of 1507 for detection purposes at any time to the competent authority.
f) The 1507 maize seeds and the products derived from line 1507 shall be specifically labeled during all stages of handling by either a label or an accompanying document with the following information:
   - the commercial name of the product, being Herculex I, the name of the GMO and its unique identification symbol;
   - the statement that "this product contains genetically modified organisms";
   - name en full address of the notifier;
   - how to access the information in the publicly accessible part of the register meant in article 31, para 2 of 2001/18/EC.
g) After the entry into force of the EU regulations on traceability / labeling (com(2001) 182) and food / feed (com(2001) 425) the notifier has to comply to these new set of regulations.
h) The consent holder should carry out monitoring according to the general surveillance plan of the notification and report on the results of the general surveillance every year, during the period the consent is valid.

Den Haag,

De Staatssecretaris van Volkshuisvesting,
Ruimtelijke Ordening en Milieubeheer,

Drs. P.L.B.A. van Geel