

**VISIT OF MR. HUGO VON MEIJENFELDT, ACTING DIRECTOR GENERAL FOR
THE ENVIRONMENT, MINISTRY OF INFRASTRUCTURE AND THE ENVIRONMENT
NETHERLANDS
TO DDG MR. LADISLAV MIKO**

15 NOV 2012, 15:00 – 16:00

Steering Note

1 Scene Setter

The Dutch Representation has requested a meeting to discuss new plant breeding technologies, plans/proposals to regulate them, and to what extent EU GMO regulation applies. The Netherlands stated that the new breeding techniques are important as they believe that they allow breeders to develop new crops faster compared to traditional breeding methods. However, they believe that the safety of the techniques used will be an important condition for any exemption, and welcome the recent two EFSA opinions in this regard (Cisgenesis, Intragenesis, Zinc-Finger-III technique).

- Dutch Researchers and Industry are interested to have some or all new plant breeding techniques out of the scope of the GMO legislation. You have discussed aspects of this issue with the Dutch company KeyGene in January 2012 in Wageningen.
- The Dutch representatives in the meeting of competent authorities for Directive 2001/18/EC have repeatedly asked the Commission for clarification on the scope. So have other Member States.
- The objective of the meeting is to explain to the Dutch representation the difficult issues at stake and to reassure that SANCO is analysing the issue.

2 Issues for Discussion

2.1 New Plant Breeding techniques

Background

- The evaluation of the GMO legislation, which the Commission published on 28 October 2011, acknowledged that pressure to update the scope of the legislation on genetic modification (GM legislation) arises in view of technical progress. The NL is an important stakeholder in this progress and is closely following the Commission's analysis of this.
- The following new techniques are of particular interest to plant breeding:
 - a. Oligonucleotide Directed Mutagenesis (ODM)
 - b. Zinc Finger Nuclease Technology (ZFN)
 - c. Cisgenesis (comprising Cisgenesis and Intragenesis)
 - d. Grafting

- e. Agro-infiltration
- f. RNA-dependent DNA methylation (RdDM)
- g. Reverse Breeding
- h. Synthetic Genomics

A short explanation of these techniques is given in the Annex.

- The Commission has recently received EFSA opinions on some of the techniques (Cisgenesis, Intragenesis, Zinc-Finger-III technique). EFSA identified the specific risks involved, compared them to the risks of already existing GMOs, and concluded that the current risk assessment guidelines can also be applied to these techniques.
- The status of the new techniques of genetic modification (in or out of scope) is currently being analysed by SANCO on the basis of a Working Group Report of Member States Experts finalised December 2011. The legal analysis is complex due to the complexity of the definition of the scope of the GM legislation, because it is old and does not match with new techniques. On this point SANCO is currently preparing a note to the legal service to clarify. The next step will be to present the legal interpretation to the Commissioner prior to presenting to Member States
- The "Plant Breeding Platform" composed of (Dow AgroSciences, Inova Fruit, Keygene N.V., Nunhems/Bayer, Rijk Zwaan, Rothamsted, Syngenta and VIB) was received three times by SANCO E1 in 2012 to present factual information and their legal analysis on new plant breeding techniques.

Suggested line to take

- Indicate that the Commission is analysing, together with the Member States' Competent Authorities, the best way forward to clarify the regulatory status of the various new techniques.
- Stress the complexity of the issue, in particular concerning the legal interpretation.
- Indicate that the Commission will present its legal interpretation to the Member States following clarification of legal issues and the agreement of the Commissioner.

Contact person: .

Tel:

Date of this version: 12 Nov 2012

Sanco officials who will attend the meeting: Dorothee Andree/HoU E1

Tel:

Annex

Short description of the new techniques

Oligonucleotide Directed Mutagenesis (ODM):

Oligonucleotides are used as template for targeted mutations. The nucleotides are delivered to the plant cells by methods like electroporation, particle bombardment, or polyethylene glycole (PEG) mediated transfection. The induced mutations are stably inherited.

Zinc Finger Nuclease Technology (ZFN); broader term: Side-Directed Nuclease Technology (SDN):

Zinc Finger Nucleases (and Side-Directed Nucleases) are specific DNA cleaving proteins. Typically, they are introduced in the plant cells and expressed transiently from a non-replicating vector. The target DNA-site depends on the number and type of zinc fingers, currently up to 24 nucleotides long. In addition, there is a DNA cleaving domain. The technique allows the introduction of site-specific mutations in the plant genome, or the site-specific integration of genes. It is worth to distinguish between ZFN-1 (random site specific mutations, as no repair template is used) and ZFN-2 (targeted site specific mutation, as a repair template is used, usually approximately 20 to 100 base pairs long) on the one side, and ZFN-3 on the other side (site specific insertion of a stretch of DNA of up to several kilo base pairs).

Cisgenesis (comprising Cisgenesis and Intragenesis):

Cisgenesis is the genetic modification of a recipient plant with a natural gene from a crossable - sexually compatible - plant. Such a gene includes its introns and is flanked by its native promoter and terminator in the normal sense orientation.

Intragenesis is the genetic modification of a recipient plant with newly aligned gene fragments from a crossable - sexually compatible - plant.

Grafting:

This old technique, used by the Chinese as early as 2000 BC, figures under new techniques, because either the scion or the (root)stock could be GM.

Agro-infiltration:

Agrobacterium sp. cells containing a T-DNA with the genetic construct of interest are infiltrated into the intercellular space of plant tissue, mostly leaves. The construct is taken up by the plant cells and is transiently expressed at high levels in the infiltrated area.

RNA-dependent DNA methylation (RdDM):

RdDM allows breeders to produce plants that do not contain foreign DNA sequences, and in which no changes in the nucleotide sequence are made. Rather, gene expression is modified epigenetically. The technique is this. First, a transgenic plant is produced where the transgene

causes DNA methylation of a specific promoter sequence, thus silencing the respective target gene. Second, the transgene is crossed out. The expression of the specific target gene remains suppressed in one or several of the subsequent generations, as long as the epigenetic methylation pattern remains stable.

Reverse Breeding:

Reverse breeding is a method in which the order of events leading to the production of a hybrid plant variety is reversed. It facilitates the production of homozygous parental lines that, once hybridised, reconstitute the genetic composition of an elite heterozygous plant, without the need for back-crossing and selection. The method of reverse breeding includes the suppression of meiotic recombination through silencing of genes following plant transformation with transgenes.

Synthetic genomics:

Synthetic genomics has been defined as "the engineering of biological components and systems that do not exist in nature and the re-engineering of existing biological elements; it is determined on the intentional design of artificial biological systems, rather than on the understanding of natural biology." (Synbiology, 2006)

Experts considered that if a synthetic entity is capable of replication or transferring genetic material it should be defined as an organism in the context of the Directive.

Synthetic genomics is a fast evolving field with potential for very new developments as compared to what can be achieved with gene modification techniques currently covered by the Directives. It will likely be used in containment (laboratories, production plants).

Synthetic Biology is currently discussed in the context of the Convention on Biological Diversity as an emerging technique which could have adverse effects on biological diversity.