Information from the Secretariat of the Biosafety Advisory Council to the readers

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PUBLIC DOSSIER

FIELD RELEASES OF TRANSGENIC PLANTS FOR EXPERIMENTAL PURPOSES

(PART B)

Fruitteeltcentrum, Katholieke Universiteit Leuven

A field assessment of the introduction of the self-compatibility trait in transgenic "Elstar" trees; flower bud formation, fruit set, yields, production efficiency and fruit quality.

B/BE/03/V1

Short Introduction:

The release of genetically modified organisms (GMOs) in the environment is strictly regulated at European level by directive 2001/18/EC of 12 March 2001, repealing directive 90/220/EEC and at Belgian level by the Royal Decree of 18 December 1998 "regulating the deliberate release and/or marketing of GMOs or products that contain GMOs into the environment". The transposition procedure is still ongoing for the moment.

To ensure the safe use of GMOs, these statues above stipulate that the release of GMOs for experimental aims is prohibited without prior permission from the competent minister. This decision is based on a thorough evaluation of the biosafety of the planned release, which is to be conducted by the Biosafety Advisory Council, which is composed of different Scientific Committees, grouping independent experts from Belgian universities and governmental institutes.

To acquire the necessary permission from the competent minister, the research centre **Fruitteeltcentrum, Katholieke Universiteit Leuven (KULeuven)**, submitted an application dossier to the Federal Service of Public Health, Safety of the Food Chain and Environment. In accordance with the advice of the Biosafety Council, the competent minister could grant a permission to the research centre **Fruitteeltcentrum, KULeuven**, to conduct experiments with transgenic **apple trees** during the years 2003 – 2006, as stipulated in the application: **B/BE/03/V1.**

The release will take place at an experimental station in **Flanders**, in the municipality of **Aarschot**, and will follow the normal growth period of crop **apple**, from **March** to **November** over a period of 4 consecutive years.

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GENERAL INFORMATION:

Description of the genetically modified Plant (GMHP) :

General Introduction: (For a list of scientific terms and phrases see Glossary).

The cultivated apple (*Malus x Domestica* .Borkh.), is an economically important fruit crop in Belgium, with a cultivated production area of 9,600 Ha. One of the problems facing apple producers however is a high annual variability in yields. For example in the period 1990 – 2001, production in Belgium varied between 140,575 and 562,382 million tonnes per year, with yields varying between 166,874 Hg/Ha and 517,895 Hg/Ha (Data from the Food and Agriculture Database of the United Nations, http://apps.fao.org/). These year-to-year differences result in large differences in income for the farmer, as well as in the price experienced by the consumer in the supermarket, and can lead to compensatory over-planting in subsequent years). These variations are at least partly due to differences in the efficiency of cross-fertilisation of flowers in Spring and the need for apple trees to cross-pollinated with pollen from another, compatible apple cultivar. Therefore most commercial orchards contain approximately 10% “pollinator” trees. The most important mechanism of cross-pollination is by the activity of honeybees. Clearly, if the weather is unfavourable during the flowering period (rain, cold etc.), then the bees will not fly and there is little cross-pollination, and decreased fruit set.

Self-incompatibility:

In this research we have been studying the activity of the gene, which is responsible for recognizing (and inhibiting) “self-pollen”, or pollen from the same or closely related variety as the mother plant. This gene is present in two copies in all apples, and is only active during flowering. It produces a small protein (an “S-RNAse”), which prevents the growth of “self-pollen” which has landed on the stigma of the flower. This gene is called the S-gene, or self-incompatibility gene.

We have isolated and copied (cloned) several of the S-genes from different varieties of apple, and then transformed leaves from the cultivated apple variety (*Malus x Domestica*. Borkh.), “Elstar” with a copy of this gene in the opposite or “antisense” direction, using a special bacterium, *Agrobacterium tumefaciens*. In nature, *Agrobacterium* is able to infect plants at places where they have been damaged or wounded. During this infection process the bacterium transfers or inserts part of its own DNA into the DNA of the plant cells at the infection site. The inserted bacterial genes result in the formation of a form of tumour or gall in the plant, in which the bacterium lives and grows. For the genetic transformation of plants, only the bacterial genes necessary for the insertion of DNA are kept, and the other genes are replaced with a new gene, e.g. in this case the S-gene. In addition to the S-gene, the *Agrobacterium* used to generate these plants also inserted a gene for resistance to the antibiotic kanamycin. This “selection” or ”marker” gene allows us to recognize and select those cells and plants that contain the inserted DNA. Therefore transgenic plants are plants that have been specifically modified in one or more genes, and with genes that might not be normally present. This differs from plants that arise as a result of sexual reproduction, in which large amounts of DNA containing many hundreds of genes from the two parents have been rearranged in a completely random manner.

Type and purpose of the envisaged trial:

The transgenic trees have already been studied for several years under controlled greenhouse conditions, and we have shown that they are either fully- or partially- self-fertile. The aim of this trial is now to see what effect the ability of an apple tree to self-fertilise has on several important agronomic traits including the yields, and the year-to-year predictability of yields in Elstar under normal field conditions. Clearly, there are much greater variations in weather conditions when the plants are grown outside. By specifically blocking only one gene activity (S-gene), we can now directly compare the normal and self-fertilizing Elstar, and actually measure the effect that the weather (cold, rain, etc.), has on fruit set, overall yields, the quality of the harvest and several other agronomic parameters. If self-fertilization can be demonstrated to improve crop yields and quality, then we can look to introduce this trait into new varieties by the classical breeding approach.

It is important to note that it is not the intention to develop commercial, transgenic apple trees from this work.

The transgenic plants used in this trial are grafted onto normal, non-transgenic rootstocks as is normal for commercial apple varieties. They are physiologically and developmentally identical to the non-transformed parent “Elstar” trees from which they were derived.

It is also important to realize that the trial is intended for experimental purposes, and all material produced (e.g. pruning wood, fruit, seeds etc., will be destroyed on site).

RESEARCH/DEVELOPMENT ACTIVITIES

Previous Development Activities

The breeding of apple varieties is a long-term process. The worked involved in this trial was started in the mid 1990's, when several versions (alleles) of the S-gene from apple were identified and their nucleotide sequence determined (Broothaerts et al., 1995;Janssens et al., 1995;Van Nerum et al., 2001;Verdoodt et al., 1998). After identification of several S-alleles, the apple cultivar "Elstar" was transformed with one of the two S-alleles naturally found in Elstar, in such a way as to suppress activity of the gene (Janssens, 1997). From 1500 transformations of Elstar leaves, 46 transformed seedlings were derived. From these transgenic shoots, seedlings were grown and characterized *in vitro* in the laboratory, before a few selected lines were multiplied and transferred to the greenhouse, where they were grafted onto a non-transgenic, commercial rootstock. These trees were grown under controlled conditions. The greenhouse trees started to flower in the Spring of 1999, and over the next few years it was possible to carry out controlled fertilizations of the flowers to determine the degree of self-compatibility of these plants.

Knowledge and experience obtained in previous development activities

Analysis of the production of fruit and seed by the transgenic lines over the last 3 years has clearly demonstrated that the transgenic lines varied from being <u>fully self-compatible </u>(self-fertile) to only <u>partially self-compatible.</u> This was also shown by the fact that pollen tube growth was no longer inhibited, and the protein produced by the S-gene (S-RNAse) was absent, or only present at a much lower level. Furthermore the plant transformation was also stable since the degree of self-compatibility remained stable over this period. Ultimately 6 different transgenic lines were selected for testing under "field" conditions, and copies (clones) of these lines copies were made by grafting buds onto a rootstock. These six lines have been thoroughly characterized at the DNA level (e.g. suppression of the S-gene expression, in different tissues including the stamens), the biochemical level (measuring the amount of protein produced by the S-gene), and the physiological level (measuring fruit production, flower formation, fruit quality flowing self- and/or cross-pollination).

Future activities:

Having thoroughly characterized the transgenic plants in the laboratory and in the greenhouse, we now want to know whether self-fertilizing plants offer a specific advantage to the farmer in the field. Although self-fertilization might only seem offer advantages, it is possible that it might result in too high a production of fruit, so that the apple fruit quality goes down, or "thinning" of the crop may need to take place.

If, as we hope, the self-compatible Elstar trees perform better than non-transformed Elstar, then we can look to introduce this characteristic into the new apple varieties we are developing, by <u>traditional</u>, classical breeding procedures. i.e several naturally-occurring self-compatible apple varieties are known, and can be used as parents in future crosses.

BENEFITS

Although a few self-fertilizing apple varieties are already available, by far the majority of commercial apples are self-incompatible. This means that when grown in monoculture for fruit production, special pollinator trees also have to be planted to ensure good cross-pollination and fruit set. In addition, the weather conditions at the time of flowering can have a dramatic effect on the efficiency of cross-pollination, and under cold, wet, cloudy or windy conditions much less pollination takes place, with a corresponding decrease in the yields. This is because cross-pollination depends mostly on the activity of honeybees, and under bad weather conditions bees will simply not fly. Therefore self-fertilizing (self-compatible) apple varieties have the potential to decrease the annual variations in yield (and farmers incomes), and to guarantee fruit production under unfavorable weather conditions, by eliminating the need for cross-pollination to produce fruit. Obviously fruit production when cross-pollinated will be unaffected. For the farmer, this also means that an additional 10% of orchard space normally reserved for pollinator trees can be planted with production trees. For the consumer this means that production, quality and end-prices will become more predictable. Over the period 1990-2001, the apple production in Belgium and Luxembourg varied by as much as 5-fold according to figures released by the Food and Agriculture Organization of the United Nations (see http://apps.fao.org/page/collections?subset=agriculture).

Although both self-compatible and parthenocarpic (fruit without fertilization) apple varieties are known, we cannot simply compare different self-compatible and self-incompatible commercial varieties, because overall yields and quality are dependent on other factors apart from fertilization efficiency alone. Furthermore the high degree of genetic diversity between apple varieties means that the only meaningful way to obtain clear answers to this question is via the transgenic approach, in which only one specific character (one gene) of the “Elstar” tree has been altered.

RISKS

It is not intended to develop transgenic, self-compatible apple trees for commercial release, the only goal of this release is to quantify the impact of self-compatibility in trees grown under field conditions over a period of several years.

The risks with the release of any transgenic plant are based on 2 main aspects, firstly the toxicity of the genes which have been introduced, and secondly the risk to the environment on the possible escape of transgenic plants or pollen/seeds.

Gene toxicities: In the trees used in this trial we have suppressed the activity of a gene (S-gene) that is naturally present in the "Elstar" apple, and which is normally expressed only during flowering. This gene is only involved in the mechanisms of rejection of self-pollen. The transgenic plants cannot therefore have any direct toxic effect on possible consumers as the S-gene is not active in the fruit of either the genetically-modified plant or the unmodified "Elstar". The transgenic lines also contain a second "marker" gene that detoxifies the antibiotics kanamycin and neomycin. This gene (*npt*II) is used as a marker during the transformation procedure to identify and select plants that have successfully been transformed. The presence or use of the *npt*II gene as a selection marker in GMOs, has been the subject of intense public debate. Independent reviews by a number of regulatory authorities have all concluded that there is no evidence to suggest that the presence of this gene in the environment leads to any toxic side effects in either humans or other animals/plants. A number of genetically modified plants that contain the *npt*II gene have also been approved for release (http://biosafety.ihe.be/ARGMO/GMO_Plants.html), (http://www.whybiotech.com/index.asp?trackid=7&id=1726#1726). Furthermore, the *npt*II gene is naturally quite widespread in nature, and is found in a number of gram-negative bacteria that are present in the soil and in the digestive tracts of animals.

Transgene escape: The greatest risk is associated with the possible escape of transgenic pollen from the site. This would then be able to cross-fertilize with other apple varieties in the area. Apple can only cross hybridize with other apples, and with quince (*Cydonia*). If this were to occur, this might mean that the transgenic escapes become partially or fully self-compatible, if they contain the same S-alleles as Elstar. As a result, once the transgenic escape has reached maturity (approx 5 – 7 years), it would be able to produce fruit by self-fertilization, if no other pollinators are present in the area. However, self-fertilization in apple is also characterized by "inbreeding depression", which results in progeny that grow poorly and are often infertile. Therefore plants containing the escaped transgene actually have a selective disadvantage since plants resulting from self-fertilization will be inbred. The plants will be unaffected in their capacity to cross-fertilize with compatible apple varieties. The presence of the antibiotic resistance gene poses no risk to the environment (since it is naturally present in bacteria of the soil and digestive tract), and offers no improvement to the survivability of the plant.

For the scientific success of the experiment it is vital that there is no escape of transgenic pollen or seed. The measures to ensure that this does not occur are detailed in the following sections.

We conclude therefore that there is no risk to either the environment or to humans.

CONTAINMENTS, CONTROL AND MONITORING MEASURES

Control of pollen dispersal (biological mixing)

The most important mechanism for cross-pollination in apples is from the activity of honeybees (many commercial orchards also contain beehives). Our own studies indicate that wind-mediated cross-pollination account a maximum of 10% of the fruit set when the pollen source is within a radius of 5m (Porta, 1996). It is furthermore essential for the scientific success of the experiment that no mixing of pollen occurs. Under field-conditions, studies have shown that very little apple pollen is found beyond a distance of 20 – 30m from the pollen source, and the recommended distance of cross-pollinating trees in an orchard to ensure efficient fertilization is every 5 – 10m (Wertheim, 1991;Williams and Smith, 1967;Wertheim, 1968). Therefore the entire field trial release site is situated at a minimum distance of 100m from the closest cross-compatible variety, located on a filed station owned and managed by K.U. Leuven. Apple can only cross-fertilise with other apple varieties and quince (*Cydonia*).

The trees will be grown in 2 "tunnels" directly next to each other. Each tunnel is 46 m long and approximately 4m high, and will contain 2 rows of trees 3m apart. Each tunnel will be protected on the sides and ends with plastic up to a height of 1.8m. One end will also contain a lockable door. The entire 2-tunnel plot will be surrounded with a 4m high windbreak, 2.5 m distance from the tunnel sides, and 6m from either end, to allow full access with a tractor. This windbreak, made of nylon netting, reduces wind speed by approximately 70%.

The top of the tunnels will be covered until over the plastic throughout the entire year with netting to exclude all pollinator insects. One week before flowering (estimated from the flower development stages), the tunnels will an additional netting (mesh size of 0.15 x 0.35 mm), to prevent pollen escape and/or entrance. This will remain in place until 1 week after the flowering period (in total approximately 5 weeks in place). Trials carried out by the FTC (Porta, 1996), have shown that when trees are covered with this gauge netting that there is a maximum 10% of the fruit set compared to insect- and wind-pollinated varieties, with pollination sources located within 5m of the test tree. With the additional windbreak in place we are confident that no pollen mixing can occur.

Under certain circumstances (e.g. in response to a period of drought or warm weather), it is possible that the trees will produce a secondary flowering later in the year. The 2 tunnels will be monitored on a weekly basis for this possibility and several times a week under conditions considered likely to promote a secondary flowering. All secondary flower buds will be manually removed at the "roosenknop" stage, collected and destroyed on site.

Control of dispersal of seeds/fruits/nuts (biological and physical mixing)

The netting covering the tunnels will serve to exclude small animals such as birds that could otherwise possibly remove apples (and seed) from the test site. As part of the scientific measurements of the experiment, all fruit produced in the test plot will be counted and measured, for size, number of seeds, position etc. All fruit that is no longer required for experimental purposes is collected by hand, and any seeds present in the fruit are removed and destroyed by soaking in sulphuric acid. The remaining flesh will be composted down. These treatments will be carried out in accordance to guidelines established in consultation with SBB (http://biosafety.ihe.be/) and OVAM (http://www.ovam.be/).

Control of volunteers (follow-up, monitoring, post-harvest treatments)

The test plot is located on property owned and managed by the K.U. Leuven. The entire station is fenced in with entry restrictions for non-personnel. By locating the test-plot here, it can be kept under constant supervision by personnel and the station manager. Entry to the test plot is restricted to personnel working on or directly involved in the project and to regulatory authorities. All visitors, treatments (sprays, pest management, pruning etc.,), are noted in a logbook maintained on-site and under supervision of the station manager.

At the end of the test period all trees will be removed and destroyed on-site by chipping, and composting down. The trees are grafted onto non-transgenic rootstock, so that there is no need to control roots in the soil. The area will be monitored in the following 2 subsequent years for the presence of any possible chance seedlings. Furthermore, the DNA from a random selection of apples (approx. 100), from the areas lying closest to the test site will be monitored annually for the presence of transgenes .

Destruction of transgenic material

All transgenic material from the test site will be collected and destroyed. Pruning wood will be chipped and either composted down or incinerated. All fruit will be composted down, after removal of the seeds, which will be soaked in sulphuric acid to prevent them from germination. Fallen leaves will be collected at the end of the season and burnt or composted down.

Once the trial has finished, the trees will be removed, and again chipped and composted down. The trees have been grafted onto a commercial (non-transgenic) rootstock. Therefore special precautions to remove root material are not required.

It is important to realize that this field trial release is for experimental purposes only. It is not the intention to utilize any of the fruit produced for feed or food purposes. The measures taken to destroy material are standard procedures for dealing with transgenic material, and should not be interpreted as been related to the toxicity of the plants, which are the same as non-transgenic apple.

Training requirements

There are no special training requirements for the personnel involved in this trial. Apart from being maintained under nettings and behind a windbreak, the trees will be treated in exactly the same way as other fruit trees in a commercial orchard. This involves for example fertilization, an integrated pest-management scheme to control the spread and development of infections (apple scab, and powdery mildew), irrigation, and pruning. The management team has additionally experience in the handling of transgenic trees under controlled greenhouse conditions.

Emergency situations

As soon as any contra-indications at the level of health and environment at test site occurs, and this will in the first instance be noticed by the personnel involved in the field trial – then the trial will be stopped. The proper authorities will be immediately informed in order to carry out further inspections. If considered necessary, all plant material will be collected and destroyed on site by chipping.

OTHER CONTAINMENT, CONTROL AND MONITORING MEASURES:

Responsibilities of the notifier:

The consent that could be given to the notifier by the competent Minister stipulates that the notifier takes complete civilian liability regarding the damage that could be caused by the deliberate release to the health of humans, animals, products of environment.

Inspection by the public authorities:

In Belgium, the Federal Service Public Health, Safety of the Food Chain and Environment is in charge of the control of the filed trials with transgenic plants. The main tasks of the inspectors regarding these kind of field trials is to inspect the trials for compliance with the conditions specified in the consent and specific protocols for growing GM crops and to investigate potential breaches of the consent. Therefore, checklists are utilized during the inspections. In order to organize its inspections, the notifier is obliged to submit exact locations of the filed trials and to inform the competent authority about the date of sowing and the date of harvesting in advance. In addition, the inspectors take samples of the plant material that are analysed in official laboratories. After harvest, the field trials are inspected on the presence of potential volunteers. In cases where mismanagement or fraud is identified specific sanctions will be imposed.

Activity report:

At the end of the growing season an activity report prepared by the notifier needs to be delivered to the competent authority, i.e. the Federal Service of Public Health, Safety of the Food Chain and Environment, before the end of that year. This activity report comprises at least the following data:

- a copy of the logbook
- the site and period of release
- the precise nature of the actually released transformants
- the actual surface area of the trial plot
- the aim(s) of the trial
- the frequency and nature of the observations on the trial plot
- the measures that were taken to prevent unwanted release of transgenic material outside the trial plot
- the method used for the destruction of the harvest and the efficacy of this
- the results obtained during the trial
- an overview of the surveillance of the plot

REFERENCES

Broothaerts, W.; Janssens, G. A.; Proost, P.; Broekaert, W. F. cDNA cloning and molecular analysis of two self-incompatibility alleles from apple. *Plant mol biol* **1995**, *27*, 499-511.

Janssens, G. Molecular analysis of the self-incompatibility (S-) gene in apple (*Malus* x *domestica* Borkh.); S-genotyping of apple cultivars and (anti)sense suppression of the S-gene, K.U.Leuven, 1997.

Janssens, G. A.; Goderis, I. J.; Broekaert, W. F.; Broothaerts, W. A molecular method for S-allele identification in apple based on allele-specific PCR. *Theoretical and Applied Genetics* **1995**, *91*, 691-698.

Porta, L. Zelf- en kruisbestuiving bij appel cv Jonagold en implicaties voor vruchtzetting en vruchtkwaliteit. Eindverhandeling voorgedragen tot het behalen van de graad van Bio-Ingenieur Landbouwkunde, K. U. Leuven, 1996.

Van Nerum, I.; Geerts, M.; Van Haute, A.; Keulemans, J.; Broothaerts, W. Re-examination of the self-incompatibility genotype of apple cultivars containing putative 'new' S-alleles. *Theoretical and Applied Genetics* **2001**, *103*, 584-591.

Verdoodt, L.; Van, H. A.; Goderis, I. J.; De, W. K.; Keulemans, J.; Broothaerts, W. Use of the multi-allelic self-incompatibility gene in apple to assess homozygosity in shoots obtained through haploid induction. *Theoretical and Applied Genetics* **1998**, *96*, 294-300.

Wertheim, S. J. Nieuwe inzichten in de bestuiving van appel en peer. *Meded. Dir. Tuinbouw* **1968**, *31*, 438-447.

Wertheim, S. J. Malus cv. Baskatong as an indicator of pollen spread in intensive apple orchards. *J Hort Sci* **1991**, *66*, 635-642.

Williams, D. R.; Smith, B. D. VII. Observations on factors influencing the effective distance of pollinator trees in 1966. *Ann. Rep. Long Ashton Agr. Hort, Res. Stn. for 1966* **1967**, 126-134.

GLOSSARY OF TERMS

Agrobacterium tumefaciens: this bacterium naturally causes certain diseases in plants, and is capable of integrating a piece of its own genetic information into the DNA of the infected plant. This procedure is used to transform plants by letting the bacteria insert a piece of DNA with the gene of interest into a plant.

Allele: one or more different forms of a particular gene, which is located on the same part of a particular chromosome.

Antibiotics: literally “anti-life”. The first antibiotics were developed from fungi (e.g. streptomycin and penicillin). Antibiotics are compounds that kill bacteria, and as such are used as medicines. In the genetic transformation of plants, antibiotics are sometimes used to distinguish between transformed cells (which also contain a gene for resistance to an antibiotic), and non-transformed cells 9which contain no resitance gene, and as a results are killed in the presence of antibiotics.

Antisense: antisense RNA (or DNA) is a single strand of nucleic acids (RNA of DNA), which is complmentary to a coding mRNA (sense). The complementary strands bind with each other, with as a result the function of the mRNA is blocked and proteins can no longer be produced.

Cloning: the creation of an organism with identical genetic information to an existing cell or living organism.

DNA: ‘deoxyribonucleic acid’, a chemical compounds that is the transmitter of an organisms heritable information. DNA consists of 2 strands of nucleotide molecules, weakly bonded to each other, and each of which is the mirror image of the other.

Enzyme: a protein that carries out he chemical reactions of metabolism in the cell.

Gene: genes serve are not only to replicate an organism, they collectively also represent the “instructions” for that organism. Each gene or a set of genes transfers this information in an inheritable manner. A gene is responsible for the synthesis of a particular protein, and therefore tells a cell what to do under particular circumstances.

Genetic modification: the directed alteration of the structure of one or more genes in a living organism through the techniques of molecular biology.

Gene expression: the degree to which the genetic information is expressed.

Genome: the complete set of genes of an organism.

GMO: “genetically modified organism”, an organism where the structure of one or more genes has been altered by the technique of genetic modification (see also “genetic modification”).

Phenotype: the observable structural and functional properties of an organism, which represents the combined integration between the genomic information of the organism with its environment.

Protein: Proteins consist of a chain of sub-units, or amino acids. Proteins are responsible for carrying out all the reactions of the living cell. The structure of individual proteins is determined directly by its gene, and each gene codes for a protein.

Recombinant organism (see *GMO*)

Resistant: not susceptible to particular diseases, insects etc.

Trait: a particular recognizable characteristic or property of the organism

Transgenic organism (see *GMO*)

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If you have any comment on the public dossier or our activities or wish to obtain additional information on the public dossier, please contact us at the following address.

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