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Datasheet for the decision of 2 February 2017

Case Number: T 1313/13 - 3.3.04

Application Number: 04814790.4

Publication Number: 1696721

IPC: C12N15/82

Language of the proceedings: EN

Title of invention:
Dominant gene suppression transgenes and methods of using same

Patent Proprietor:
Pioneer Hi-Bred International, INC.

Opponent:
Syngenta Crop Protection AG

Headword:
Method for the production of maintainer plants/PIONEER

Relevant legal provisions:
EPC Art. 56, 84, 123(2), 123(3)
EPC R. 115(2)
RPBA Art. 15(3)

Keyword:
Auxiliary request 4 - requirements of the EPC met (yes)

Decisions cited:

Catchword:

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Case Number: T 1313/13 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 2 February 2017

Appellant: (Opponent)	Syngenta Crop Protection AG Schwarzwaldallee 215 4058 Basel (CH)
Respondent: (Patent Proprietor)	Pioneer Hi-Bred International, Inc. 9550 White Oak Lane, Suite 100 Johnston, Iowa 50131-1014 (US)
Representative:	Bentham, Andrew J A Kemp 14 South Square Gray's Inn London WC1R 5JJ (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 28 March 2013 concerning maintenance of the European Patent No. 1696721 in amended form.**

Composition of the Board:

Chairwoman	G. Alt
Members:	M. Montrone
	M.-B. Tardo-Dino

Summary of Facts and Submissions

I. An appeal was lodged by the opponent (hereinafter "the appellant") against the interlocutory decision of the opposition division maintaining European patent No. 1 696 721 in amended form. The patent is based on European application No. 04 814 790.4, which was filed as international application and published as WO 2005/059121 (hereinafter "the application as filed"). The patent has the title "*Dominant gene suppression transgenes and methods of using same*".

II. The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty and inventive step, and under Articles 100(b) and 100(c) EPC.

III. In the impugned decision the opposition division held that the subject-matter of claims 1 of the main request and auxiliary requests 1 and 2 related to added subject-matter, while claim 1 of auxiliary request 3 described "*subject-matter within the exceptions to patentability as defined in Article 53(b) EPC and G2/07*". Furthermore, it took the view that the subject-matter of claims 1 of auxiliary requests 4 and 5 was obvious in the light of the teaching of document D1 (see section VII below) and that the patent in suit did not disclose the invention defined in claim 1 of auxiliary request 6 in a manner sufficiently clear and complete for it to be carried out by the skilled person.

Auxiliary request 7 was held to meet the requirements of the EPC.

Claim 1 of this request reads:

"1. A method of producing a maintainer plant, comprising introducing by transformation into a second maize plant an exogenous restoring gene construct comprising

(i) a first nucleotide sequence that, if introduced into a first maize plant with a homozygous recessive genotype for a trait that affects viability or fertility, wherein the trait is male sterility, would restore the homozygous recessive trait, said first nucleotide sequence being in a hemizygous condition;

(ii) a second nucleotide sequence, linked to the first nucleotide sequence, which inhibits the formation, function, or dispersal of male gametes of the maintainer plant, wherein the second nucleotide sequence is operably linked to a promoter preferentially directing expression in the male gametes;

wherein the maintainer plant further comprises a third nucleotide sequence linked to the first nucleotide sequence and encoding a scorable visual marker product capable of being used for selection of progeny seed comprising the restoring gene construct;

wherein the first nucleotide sequence restores male fertility sporophytically".

The decision under appeal did not give a detailed assessment of inventive step for auxiliary request 7, but it is apparent from the context that the same reasoning as that put forward for auxiliary request 6

was intended to apply. The disclosure in document D1 represented the closest prior art for the subject-matter of claim 1, and the difference between the two was that the construct comprised a sequence encoding a visual marker. The technical problem was formulated as the "*provision of an improved maintainer plant*". The opposition division held that document "*D1 does not suggest the use of a visual marker for allowing selection of seeds*" and therefore considered the subject-matter of the claims to involve an inventive step.

IV. With its statement of grounds of appeal the appellant filed documents D23 and D24 (see section VII below). The appellant challenged the impugned decision solely on the ground of lack of inventive step (Article 56 EPC) of the subject-matter of claims 1 to 4 of auxiliary request 7. It took the view that, contrary to the finding of the opposition division, claim 1's feature "*comprises a third nucleotide sequence linked to the first nucleotide sequence and encoding a scorable visual marker product capable of being used for selection of progeny seed comprising the restoring gene construct*" (hereinafter the "scorable visual marker" feature) was obvious from the teaching of document D1 "*either alone or in combination with document D3*", when taking account of either of documents D23 or D24. No reasoning was provided for the alleged lack of inventive step in the light of a combination of the disclosure of documents D1, D3 (see section VII below) and either of documents D23 or D24.

V. In reply to the statement of grounds of appeal the patent proprietor (hereinafter "the respondent") submitted a main request which was identical to auxiliary request 7 underlying the impugned decision,

and five auxiliary requests. The respondent furthermore requested that documents D23 and D24 be excluded from the proceedings as inadmissible.

VI. The parties were informed of the board's preliminary view in a communication pursuant to Article 15(1) RPBA. The board indicated *inter alia* that it was minded to admit documents D23 and D24 into the appeal proceedings and that it agreed with the parties that document D1 represented the closed prior art.

VII. The following documents are cited in this decision:

D1: US5750867

D3: Cigan A. M. et al., Sex Plant Reprod., 14, 135 to 142, 2000

D23: EP0198288

D24: US4727219

VIII. Oral proceedings before the board were held on 2 February 2017, in the absence - as announced - of the duly summoned appellant. At these proceedings the board decided not to exclude documents D23 and D24 pursuant to Article 12(4) RPBA. The respondent withdrew all pending requests except auxiliary request 4 (which had been filed as auxiliary request 2 with the reply to the appellant's statement of grounds of appeal). At the end of the oral proceedings the chairwoman announced the board's decision.

Claims 1 to 4 of auxiliary request 4 read:

"1. A method of producing a maintainer plant, comprising introducing by transformation into a second maize plant an exogenous restoring gene construct comprising

(i) a first nucleotide sequence that, if introduced into a first maize plant with a homozygous recessive genotype for a trait that affects viability or fertility, wherein the trait is male sterility, would restore the homozygous recessive trait, said first nucleotide sequence being in a hemizygous condition;

(ii) a second nucleotide sequence, linked to the first nucleotide sequence, which inhibits the formation, function, or dispersal of male gametes of the maintainer plant by interference with the normal accumulation of starch in pollen, wherein the second nucleotide sequence is operably linked to a promoter preferentially directing expression in the male gametes;

wherein the maintainer plant further comprises a third nucleotide sequence linked to the first nucleotide sequence and encoding a scorable visual marker product capable of being used for selection of progeny seed comprising the restoring gene construct;

wherein the first nucleotide sequence restores male fertility sporophytically.

2. The method of claim 1 wherein said first nucleotide sequence is MS45.

3. The method of claim 1 wherein said first nucleotide sequence is SBMu200, BS92-7, MS1 or MS2.

4. The maintainer maize plant of Claim 1 which, if self-fertilised, produces progeny in a 50:50 male-sterile:male-fertile ratio."

IX. The appellant's arguments in writing were only directed to the request found allowable by the opposition division, i.e. auxiliary request 7. No arguments were submitted with regard to the request finally maintained by the respondent, auxiliary request 4 (filed as auxiliary request 2 with the reply to the statement of grounds of appeal), and none of the arguments submitted in relation to auxiliary request 7 apply to this request.

X. The respondent's arguments may be summarised as follows:

Admission of documents D23 and D24 into the appeal proceedings

Documents D23 and D24 could and should have been filed during the first-instance proceedings, and at the appeal stage they were thus late-filed. Both documents had been filed with regard to the "scorable visual marker" feature referred to in claim 1, which feature, however had already been referred to in claim 9 as granted and had therefore been present since the beginning of the opposition proceedings. The fact that both documents were referred to in document D1 was a further indication that they were known to the appellant and should therefore have been filed during the first-instance proceedings.

Auxiliary request 4

Inventive step (Article 56 EPC)

Document D1 represented the closest prior art. It disclosed a method for the production of maize maintainer plants which relied on the transformation of plants with a genetic construct comprising a fertility-restorer gene linked to a pollen-lethality gene and a transformation selection marker (column 3, lines 23 to 65, column 6, lines 41 to 48). Pollen-lethality genes were defined as molecules that, when expressed, significantly disrupted the metabolism, functioning and/or development of microspores and pollen. Explicitly reported examples were the ribonuclease (RNAse) enzymes barnase and RNase T1 (see e.g. column 6, lines 37 to 48, column 14, lines 60 to 64). The toxic activity of the pollen-lethality genes was controlled by their selective expression in pollen or microspores mediated by pollen-specific promoters (see column 6, lines 49 to 61). It was commonly known that RNAses exerted their cytotoxic activity by degradation of RNA molecules, i.e. of molecules which primarily encoded proteins. Proteins were essential compounds in all plant tissues, which meant that when the pollen-specific promoter was leaky, i.e. active in non-pollen specific tissues, the construct was toxic for the transformed maintainer plants too.

The subject-matter of claim 1 differed from the method disclosed in document D1 *inter alia* in that it referred to a pollen-lethality gene which interfered with the accumulation of starch. This approach was more specific for pollen, since it relied on enzymes which specifically degraded starch. Starch was vital for the development of fertile pollen, while a lack of starch

was less toxic for other plant tissues. This improved the production of maintainer plants since fewer plants were killed when the pollen-specific promoter was leaky.

The technical problem was thus the provision of an improved method for the production of maintainer plants.

Document D1 suggested neither a construct which interfered with starch accumulation in the suppression of pollen fertility in the production of maize maintainer plants nor the advantages associated with this approach, i.e. a higher pollen specificity combined with a lower toxicity for the other plant tissues. This was also not hinted at by combining the teaching of document D1 with that of any of the other cited prior art documents. Thus, the subject-matter of claim 1 was not obvious and therefore met the requirements of Article 56 EPC.

XI. The appellant requested in writing that the decision under appeal be set aside and that the patent be revoked in its entirety.

The respondent requested that the patent be maintained on the basis of auxiliary request 4, corresponding to auxiliary request 2 filed with the reply to the statement of grounds of appeal.

Reasons for the Decision

1. The duly summoned appellant did not attend the oral proceedings, which in accordance with Rule 115(2) EPC

and Article 15(3) RPBA, took place in its absence. Auxiliary request 4 on which the present decision is based was submitted as auxiliary request 2 with the respondent's reply to the appellant's statement of grounds of appeal. The appellant had had therefore an opportunity to submit comments with regard to this request.

Admission of documents D23 and D24 into the appeal proceedings (Article 12(4) RPBA)

2. In view of the board's decision on inventive step which is in the respondent's favour (see below), the board sees no necessity to provide detailed written reasons for its decision at the oral proceedings to dismiss the respondent's request to exclude documents D23 and D24 from the proceedings.

Introduction to the invention

3. The invention concerns a method for the production of "maintainer plants" by transgenic means. Maintainer plants are needed for plant breeding purposes, to restore the fertility in either male- or female-sterile parental plants which are genetically identical to the maintainer plants except for their sterility trait. The maintainer plants function as pollen or female plant donors to the sterile parental plant lines in order to ensure their maintenance.

4. The sterility of the two parental plants is of economic importance since it prevents the plants from self-pollination("selfing") in the field, thereby fostering the homogeneous generation of hybrid plants. Hybrid

plants generally exhibit improved agronomic characteristics, for example in yield and vigour, compared to their parental plants.

Auxiliary request 4

Amendments (Article 123(2) EPC), extension of protection (Article 123(3) EPC), clarity and support (Article 84 EPC)

5. Claim 1 of auxiliary request 4 differs from that of auxiliary request 7 underlying the impugned decision in that the feature "by interference with the normal accumulation of starch in pollen" has been added to part (ii). Claims 2 to 4 of both requests are identical.

6. The board notes that the amendment in part (ii) of claim 1 has a word-for-word basis on page 61, lines 9 to 11 of the application as filed. Furthermore, it is evident that this amendment adds a further technical feature to the subject-matter of claim 1 - compared to that of claim 1 as granted - thereby restricting the extent of protection. Lastly, the amendment relates to a functional feature which is considered to have a clear and unambiguous meaning for the skilled person in the art and is supported in the description.

7. Therefore, auxiliary request 4 meets the requirements of Articles 84 and 123(2) and (3) EPC.

Inventive step (Article 56 EPC)

Closest prior art

8. The board agrees with the parties that document D1 represents the closest prior art for the subject-matter of claim 1.

9. Document D1 discloses a method for producing maintainer maize plants by transforming the plants with a genetic construct comprising (i) a fertility-restorer gene for a homozygous recessive male sterility trait, (ii) a pollen-lethality gene which is selectively expressed in male gametes, and (iii) a selection marker (see e.g. column 3, lines 23 to 65, column 6, lines 29 to 32, example 2). Pollen-lethality genes encode molecules which, when expressed, significantly disrupt the metabolism, functioning and/or development of microspores and pollen. Explicitly reported examples are the ribonuclease (RNAse) enzymes barnase and RNase T1 (see e.g. column 6, lines 37 to 48, column 14, lines 60 to 64). RNAses are commonly known to exert their cytotoxic activity by degrading all types of RNA molecules, which under non-degrading conditions are primarily translated into proteins, i.e. essential components of all plant tissues. Therefore, the gene encoding an RNAse is linked to a pollen-specific promoter to restrict its cytotoxic activity to pollen tissues (see e.g. column 6, lines 49 to 61, column 14, lines 63 and 64). Genes encoding agents that interfere with starch accumulation in pollen are not disclosed in document D1.

Technical problem and solution

10. The subject-matter of claim 1 differs from the method disclosed in document D1 at least in that the pollen-lethality genes encode agents which interfere with starch accumulation in pollen. This difference will be considered in the following.

11. The patent in suit discloses that, for example, genes encoding α- or β-amylases which degrade starch when operably linked to a pollen-specific promoter selectively prevent starch accumulation in maize pollen. Starch is a storage product which is essential for the development of fertile maize pollen (see e.g. example 9), but not necessarily vital for other maize plant tissues. Pollen-specific promoters which control the cytotoxic activity of pollen-lethality genes - in this case, genes encoding enzymes that interfere with starch accumulation or RNases that degrade RNA - by restricting their gene expression to pollen may become leaky, *i.e.* the genes under their control may also be expressed in non-pollen tissues of plants. The extent of cytotoxic effects mediated by these genes in the event of an unspecific expression relies on the target molecules affected, and in particular on how essential they are for the vitality of the plant tissues. RNases degrade RNA molecules which encode primarily proteins, i.e. molecules essential for all plant tissues (see point 9 above), while starch as a mere storage product is primarily essential for the development of mature pollen. Therefore, an approach which, in the event of a leaky pollen-specific promoter, selectively affects the vitality of pollen while leaving other plant tissues almost unaffected may increase the amount of maintainer plants produced, because potential losses due to leaky pollen-specific promoters are reduced.

12. Hence, the technical effect associated with the distinguishing feature referred to in point 10 above is that more maintainer plants are produced.

13. The objective technical problem to be solved is thus the provision of an improved method for the production of maintainer plants.

14. The board is satisfied that the subject-matter of claim 1 solves this problem in view of the patent's disclosure (see e.g. example 9) of enzymes capable of specifically interfering with starch accumulation in pollen.

Obviousness

15. It has to be assessed whether or not the skilled person, starting from the method of producing maintainer plants that is disclosed in document D1 and faced with the technical problem defined above, would modify the teaching of document D1 - either alone or in combination with that of other the prior art - to arrive at the claimed subject-matter in an obvious manner.

16. The board notes that document D1 discloses in general terms that pollen-lethality DNAs "*preferably encode an RNA and/or a protein or polypeptide that, when expressed in microspores or pollen, significantly disrupts their metabolism, functioning and/or development*" (see column 6, lines 38 to 41). RNAses are the only specific examples disclosed (see e.g. example 2). Accordingly, neither the general disclosure in document D1 with regard to pollen-lethality genes nor the exemplified RNases due to their fundamentally

different target specificity (see point 9 above) provide pointers to the skilled person to use, as pollen-lethality genes, those that selectively interfere with starch accumulation.

17. Thus, the feature "by interference with the normal accumulation of starch in pollen" and consequently the subject-matter of claim 1 as a whole is not obvious in the light of the teaching of document D1 alone.

18. With regard to documents D23 and D24, which were submitted by the appellant with its statement of grounds of appeal, the following is noted.

18.1 Document D23 discloses marker systems which are brought by transformation means into the close proximity of a target locus, for example, male sterile or fertile chromosomal loci (see abstract, column 6, lines 34 to 38, column 11, lines 14 to 31). As markers, the document discloses *inter alia* dominant conditional lethal markers, i.e. enzymes which convert externally added non-toxic precursor compounds intracellularly into toxic products (see column 8, line 8, column 12, lines 12 to 20, column 14, line 17 to column 15, line 40). However, the document discloses no pointers to non-conditional lethal markers, let alone to enzymes that interfere with starch accumulation in pollen and their potential use in the production of maintainer plants.

18.2 Document D24 discloses methods for the production of male-sterile maize plants wherein visual marker genes are closely linked to chromosomal male sterility loci which allow a fast selection of suitable breeding candidates (see e.g. abstract, claim 1, column 5, line 61 to column 6, line 7, column 6, lines 50 to 68). The

document discloses no pointers to selection markers which cause lethality, let alone to enzymes that interfere with starch accumulation in pollen and their potential use in the production of maintainer plants.

19. Hence, the board concludes that the feature "by interference with the normal accumulation of starch in pollen" and hence the subject-matter of claim 1 as a whole likewise cannot be considered obvious in the light of the teaching of document D1 combined with that of documents D23 or D24. The same applies to the subject-matter of claims 2 and 3 dependent thereon and to the maintainer plant according to claim 4.

20. As noted above, the appellant did not submit arguments regarding the feature "by interference with the normal accumulation of starch in pollen", which is now present in claim 1 of auxiliary request 4, but was not present in auxiliary request 7. The only arguments submitted in writing by the appellant concerned the latter request and therefore there is no need for the board to consider them (see point 5 and section IX above).

21. Thus, auxiliary request 4 meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the basis of auxiliary request 4, corresponding to auxiliary request 2 filed with the reply to the statement of grounds of appeal, and a description to be adapted thereto.

The Registrar: The Chairwoman:

L. Malécot-Grob G. Alt

Decision electronically authenticated