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Datasheet for the decision of 10 January 2013

Case Number: T 2239/08 - 3.3.08

Application Number: 99971448.8

Publication Number: 1127106

IPC: C12N 15/82, A01H 5/10

Language of the proceedings: EN

Title of invention:
Glufosinate tolerant rice

Applicant:
Bayer CropScience NV

Opponent:
-

Headword:
Rice/BAYER

Relevant legal provisions:
EPC Art. 53(b), 56, 84, 123(2)

Keyword:
"Elite event with elements of surprise created in a non-obvious way: inventive step (yes) - see points (10) - (21)"

Decisions cited:
G 0001/98, T 0775/08

Catchword:
-

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Case Number: T 2239/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 10 January 2013

Appellant: (Applicant)
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 20 June 2008 refusing European patent application No. 99971448.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: T. J. H. Mennessier
J. Geschwind

Summary of Facts and Submissions

I. The applicant (appellant) lodged an appeal against the decision of the examining division of 20 June 2008, whereby the European patent application No. 99 971 448.8 with publication number 1 127 106 was refused. The application, entitled "*Glufosinate Tolerant Rice*", originated from an international application published as WO 00/26345.

II. The decision was based on the main request and auxiliary requests I to III all filed at the oral proceedings of 10 June 2008. All four requests were refused for reasons of non-compliance with the requirements of Article 56 EPC.

III. The statement setting out the grounds of appeal was filed on 30 October 2008. It was accompanied by a new main request and four new auxiliary requests.

IV. On 19 September 2012, the Board issued a communication, pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), sent together with the summons to oral proceedings, in which it expressed its provisional, non-binding views.

V. On 10 December 2012, in reply to the Board's communication, the appellant filed additional submissions which were accompanied by a new main request and three new auxiliary requests to replace the previous requests, and by three new documents including document D11 (see Section VIII, below).

VI. At the oral proceedings, which took place on 10 January 2013, the appellant withdrew the requests filed on 10 December 2012 and submitted as its sole request a new main request which consisted of two claims.

VII. Claims 1 and 2 of the new main request read:

"1. A transgenic, glufosinate rice plant, cell, tissue or seed, comprising in its genome a PvuI-HindIII 1501 base pair 35S-*bar* transgene comprising the genetic elements shown in the Table of Example 1a) and wherein said 35S *bar* transgene is located between a 92 nucleotide upstream flanking region and a 675 nucleotide downstream flanking region, said upstream region being located immediately upstream of and contiguous with said transgene and comprising the nucleotide sequence designated YTP059:

5'-TCGGACAACCGCGATAGTTCG-3'

in position 56-76 of the upstream flanking region and said downstream flanking region being located immediately downstream of and contiguous with said transgene, and comprising the nucleotide sequence complementary to the sequence designated OSA04:

5'-TCGCATATGTATGTAACACGC-3'

in position 93-113 of the downstream flanking region, the transgenic elements shown in the Table of Example 1a) being present in the rice Elite Event GAT-OS2 deposited with the ATCC with the accession number ATCC 203352."

"2. A process for cultivating rice plants which comprises growing plants of claim 1 and applying a herbicide with glufosinate as an active ingredient to the cultivated rice plants."

VIII. The following documents are referred to in the present decision:

(D1) J.H. Oard et al., Molecular Breeding, Vol. 2, 1996, pages 359 to 368

(D2) S.K. Datta et al., Plant Molecular Biology, Vol. 20, 1992, pages 619 to 629

(D11) Declaration of Frank Michiels dated 5 December 2012

IX. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows:

Admissibility of the request filed at the oral proceedings

The request was filed in reaction to objections under Article 84 EPC raised for the first time at the oral proceedings. Therefore, it should be admitted into the proceedings.

Admissibility of document D11

Document D11 which was a declaration of an inventor was submitted in direct reply to the Board's communication pursuant to Article 15(1) RPBA. It contained data confirming the disclosure of the invention in the application in suit. Therefore, it should be admitted into the proceedings.

Article 123(2) EPC

The claimed subject was disclosed in the application as filed. Support could be found in particular on pages 17 and 23 to 26 and in claims 12 and 13 as filed.

Article 56 EPC

Document D1 represented the closest prior art. It described field trials with 15 transgenic rice plant lines, allegedly representing 11 independent rice transformation events generated upon transformation of the parental cultivars with a plasmid containing inter alia a chimeric *bar* gene. None of these transgenic rice events qualified as a transformation event with characteristics similar to the GAT-OS2 event contained in the plants and biological material derived therefrom according to claim 1, in that the transgenic lines of document D1 did not combine glufosinate tolerance with optimal overall agronomic performance, genetic stability and adaptability to different genetic backgrounds. The Koshihikari derived lines did not contain a commercially acceptable expression level (resulting in herbicide tolerance) in a range of environmental conditions to which the plants carrying the event were likely to be exposed in normal agronomic use. Figure 3 showed that all the transgenic lines tested suffered at least 10% injury due to the herbicide treatment. Document D1 did not indicate how the transgenes were inherited. At least 6 transgenic lines did not reveal any hybridisation with the *bar* gene in a southern blot test. A variation for all agronomic traits was observed within lines indicating that the transformation events of document D1 were not neutral with regard to agronomic performance of

transgenic lines. Furthermore, the use of traditional breeding methods to identify transgenic lines having at least the agronomic performance of the original patent was suggested.

In the light of the disclosure in document D1, the technical problem underlying the present application was seen as the provision of transgenic rice plants having, in combination with glufosinate tolerance, optimal overall agronomic performance, genetic stability and adaptability to different backgrounds.

In document D2, the transgenic plants generated upon transformation using a chimeric *bar*-gene did not seed and showed male sterility. Therefore, the transformation events described therein were not neutral with respect to agronomical performance of the plants in which they were contained.

The GAT-OS2 event contained in the plants and biological material derived therefrom according to claim 1 resulted from the transformation of the parental plants using a definite fragment of 1501 base pairs containing essentially a chimeric *bar*-gene, contrary to documents D1 and D2 which used a complex plasmid. The use of such a genetic construct was not suggested by any of the prior art documents. Moreover, as emphasised in document D11, which confirmed the disclosure in the application, the transgenic plants of claim 1 surprisingly combined glufosinate tolerance with optimal overall agronomic performance, genetic stability and adaptability to different genetic backgrounds.

X. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of claims 1 to 2 and the main request filed at the oral proceedings.

Reasons for the Decision

Admissibility of the new main request

1. The main request was filed at the oral proceedings held on 10 January 2013. The claims of this request differ from the claims of auxiliary request II filed under cover of the letter of 10 December 2012, in so far as they respond to some objections under Article 84 EPC, raised for the first time by the Board at the oral proceedings. The Board, therefore, exercising its discretion according to Article 13(1) RPBA, decides to admit this request into the procedure.

Admissibility of document D11

2. Document D11 is a declaration of an inventor providing extracts of data obtained by the inventors in the identification and characterisation of GAT-OS2 as summarised in the application. The document was submitted in preparation of the oral proceedings by the appellant in its efforts to make a full statement of the grounds why the revision of the contested decision was requested. The Board, therefore, exercising its discretion according to Article 13(1) RPBA, decides to admit document D11 into the procedure.

Article 123(2) EPC

3. Support for the plant and biological material derived therefrom of claim 1 is found in the application as filed (see the published international application). The relevant passages are as follows:

(a) The precise structure of the PvuI-HindIII 1501 base pair 35S-bar transgene is described on page 17.

(b) The 92 nucleotide downstream- and 675 nucleotide upstream regions flanking the GAT-OS2 event are described on pages 23 to 25 (see in particular page 24, lines 13 to 16 and page 25, lines 6 to 8).

(c) The primer YTP059 is described on page 26 (see top).

(d) The nucleotide sequence complementary to the sequence OSA04 can be derived directly from the sequence of said primer given page 29, line 9.

(e) The exact position (56 -> 76) of the nucleotide sequence YTP059 in the 5' flanking region is given at the top of page 26.

(f) The exact position of the nucleotide sequence complementary to the sequence OSA04 from nucleotide 93 to nucleotide 113 in the downstream flanking region can be directly derived from the data given at pages 25 and 26. Page 25 refers to a 1279 bp fragment - obtained upon amplification with primers MDB285 and MDB410 - (see the Table

and lines 6 to 8), whose sequence from nucleotide 1 to nucleotide 604 belongs to the inserted transgene while nucleotide 605 is the first nucleotide of the plant DNA. From the top of page 26 it can be extrapolated that the sequence complementary to OSA04 starts at nucleotide 697 of the 1279 bp fragment and finishes at nucleotide 717 of the same. By simply subtracting 604 nucleotides from theses figures, one arrives at positions 93 and 113.

(g) The presence of the GAT-OS2 event in the seeds deposited at the ATCC under number ATCC 203352 is indicated on page 14, lines 10 to 11.

(h) A transgenic rice plant, cell, tissue or seed containing the event GAT-OS2 is described on page 4, lines 16 to 20.

4. Support for the process for cultivating rice plants of claim 2 is found in claims 12 and 13 as filed.

5. Therefore, the Board is satisfied that the main request meets the requirements of Article 123(2) EPC.

Article 84 EPC

6. The Board is satisfied that, owing to the amendments carried out to define the subject-matter of claim 1, the main request complies with the requirements of Article 84 EPC.

Article 83 EPC

7. The Board is further satisfied that the invention according to claim 1 is sufficiently disclosed and concludes that the main request complies with the requirements of Article 83 EPC.

Article 53(b) EPC

8. It is acknowledged that the rice plant containing the elite event GAT-OS2 deposited with ATCC accession number 203352 is a specific rice variety which, as such, is excluded from patent protection by Article 53(b) EPC and Rule 27(b) EPC (cf. G 1/98, OJ EPO 2000, page 111). However, the subject-matter of claim 1 is not limited to the specific deposited rice variety but encompasses all possible rice varieties having in their genome the genetic elements shown in the Table of Example 1a and the 5' and 3' flanking regions spanning the insertion site comprising the nucleotide sequences designated YTP059 (downstream) and OSA04 (upstream), and does therefore not fall under the exclusion of Article 53(b) EPC.

Article 54 EPC

9. The method according to claim 1 is not disclosed in any of the prior art documents on file and is therefore novel within the meaning of Article 54 EPC.

Article 56 EPC

10. Document D1 represents the closest state of the art. It summarizes results of extensive field tests over two

consecutive years to evaluate stability and agronomic performance of *bar*-containing transgenic rice lines with and without glufosinate treatments. The rice lines had been generated from the commercial cultivars 'Gulfmont' and 'Koshihikari' upon electric discharge particle bombardment to express the *bar* gene (see the abstract on page 359). The transformation was carried out using a complex plasmid containing, in addition to the *bar*-transgene, two other transgenes (with respectively a aphIV coding region and a uidA coding region). The chimeric *bar*-gene contained the *bar* sequence driven by the CaMV 35S promoter, together with the nopaline synthase terminator (see page 360, bottom of right-hand column). Fifteen lines representing 11 independent transformation events were analysed by performing Southern blots. At least 8 different integration patterns were revealed for the *bar* transgene (see page 363, Section 'Results and Discussion). One Southern blot (see Figure 1, Blot B, on page 363) shows that at least 6 transgenic lines did not reveal any hybridization when probed with the *bar* gene. This observation raises questions as to whether the *bar* transgene was stably inherited. Whereas Gulfmont derived transgenic lines displayed no visible injury due to herbicide treatments, all Koshihikari lines exhibited initial yellowing and some stunting 2 to 3 days after glufosinate application (see page 364, right-hand column, first paragraph). Figure 3 (see page 365) shows that all transgenic lines suffered at least 10% injury. Grain yields for 33% of the Koshihikari lines were significantly reduced with increasing glufosinate rates. The authors contend that variation for grain yield among transgenic lines could be explained by position effects of the *bar* or *uidA*

transgenes (see page 364, right-hand column, second paragraph). Transgenic Gulfmont lines were in general more glufosinate resistant than the Koshihikari lines which suggested that genetic background played a role in expression of the transferred *bar* gene. The authors conclude that the significant variation for all agronomic traits observed within lines was most probably the result of position effects of integrated transgenes and state that plant traditional breeding methods are still required to identify transgenic lines that are equal in agronomic performance to the original parental cultivar (see the conclusion on page 367 to 368 and the abstract on page 359).

11. In view of the above comments, the Board observes that, in the transgenic rice plants of document D1, (i) glufosinate treatment is associated with injuries of the plants (sign of a lack of glufosinate tolerance), (ii) the *bar*-transgene failed to be stably integrated at a definite insertion site of the genome (sign of a lack of genetic stability), (iii) the agronomic performance suffers from variability (sign of a lack of optimal overall agronomic performance) and (iv) expression of the *bar*-transgene is influenced by the genetic background (sign of a lack of adaptability to different backgrounds).

12. In the light of the disclosure in document D1, the technical problem underlying the present application is seen as the provision of transgenic rice plants having, in combination with glufosinate tolerance, optimal overall agronomic performance, genetic stability and adaptability to different backgrounds. As a solution to this problem, the application proposes the transgenic

plants (and cells, tissues or seeds thereof) according to claim 1 which rely on the integration at a definite site in the rice genome of a definite PvuI-HindIII 1501 base pair 35S-bar transgene. Considering the disclosure in the experimental part of the description and the additional information provided by the declaration of F. Michiels (document D11), the Board is convinced that the technical problem has credibly been solved by the claimed method.

13. In view of the experimental results presented both in the description and in document D11 (see points 15 and 16 below) the Board, in the absence of any evidence to the contrary, has no reason to question the appellant's assertion that any transgenic rice plant containing the GAS-OS2 event will combine glufosinate tolerance with optimal overall agronomic performance, genetic stability and adaptability to different backgrounds.

14. It remains to be answered whether, starting from the method of document D1 and in view of the prior art documents on file, a skilled person would have arrived at the claimed solution in an obvious way. The Board will also assess whether the claimed plants contain elements of surprise which in addition may justify the recognition of an inventive step.

15. In decision T 775/08 of 1 February 2011, the same Board in a different composition has assessed whether the provision of (alfalfa) plants with high tolerance to a herbicide (glyphosate) containing an elite event was inventive. In this case, the prior art provided a clear guidance to the skilled person for obtaining glyfosate tolerant alfalfa plants. The Board decided that the

combination of physiological and morphological characteristics associated with the presence of a high glyphosate tolerance, none of them having been addressed by the examining division or found in the prior art, was an element of surprise justifying the acknowledgment of inventive merit.

16. In the present case, the examining division considered that the skilled person, in order to solve the problem, would have turned to document D2 which reported results of field tests which were conducted with transgenic lines derived from the rice cultivar IR72 using a 3996 base pair plasmid containing the *bar* gene (see document D2, page 624, Figure 2).

17. The Board disagrees. As the transformation gave rise to transgenic plants which did not set seeds and showed male sterility (see page 624, left-hand column, first paragraph), the skilled person would have paid no attention to the teaching of document D2.

18. In addition, in contrast to the teaching of both documents D1 and D2 using complex plasmids, the transgenic plants according to claim 1 were generated using a definite fragment of 1501 nucleotides containing essentially the bar-gene driven by the CaMV 35S promoter instead of a complex plasmid. There was no suggestion in any of the cited prior art documents that the transformation of rice plants with such a genetic construct would be successful with a Mendelian inheritance of the transgene at a single locus in at least three subsequent generations indicating that the insert is stably integrated (see Example 3, page 26,

lines 10 to 22 in the application and Table 3 of document D11).

19. Moreover, the resulting transgenic rice plants surprisingly exhibit not only glufosinate tolerance (see Example 2 of the application, and Tables 6 and 7 of document D11) but also optimal overall agronomic performance (see Example 2 and page 2, lines 28 to 30 in the application, and Tables 4 to 12 of document D11) and adaptability to different genetic backgrounds (see Example 4 of the application and Table 13 of document D11).

20. The Board concludes that the skilled person facing the technical problem as defined at point 12 (see above) would not have arrived in an obvious way at the solution of claim 1, i.e. at plants, or biological material derived therefrom, comprising the chance elite event GAT-OS2.

21. Thus, the subject-matter of claim 1, as well as of dependent claim 2, involves an inventive step. Therefore, the main request complies with 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 examining division with the order to grant a patent on the basis of claims 1 to 2 of the main request filed at the oral proceedings and the description yet to be adapted thereto.

The Registrar The Chairman

A. Wolinski M. Wieser