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Datasheet for the decision of 3 May 2013

Case Number: T 1254/10 - 3.3.08

Application Number: 04789084.3

Publication Number: 1664311

IPC: C12N 15/82, A01H 5/00

Language of the proceedings: EN

Title of invention:
Actin regulatory elements for use in plants

Applicant:
Monsanto Technology LLC

Headword:
Rice actin promoter/MONSANTO

Relevant legal provisions:
EPC Art. 123(2), 56
RPBA Art. 13(1)

Keyword:
"Admissibility of Main Request and first and second Auxiliary Request (yes)"
"Added subject-matter (no)"
"Inventive step (no)"

Decisions cited:
-

Catchword:
-

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Case Number: T 1254/10 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 3 May 2013

Appellant: (Applicant)
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Representative:
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 11 January 2010 refusing European application No. 04789084.3 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
R. Moufang

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division dated 11 January 2010 whereby the European patent application No. 04 789 084.3, published as International patent application WO 2005/030968 (hereinafter "*the application*"), was refused.

II. The examining division considered the set of nine claims filed with a letter dated 12 June 2008 not to fulfil the requirements of Articles 123(2) and 56 EPC. Claims 1 and 7 of this request read as follows:

"1. A DNA construct comprising an isolated polynucleotide molecule comprising

(i) a polynucleotide sequence represented by SEQ ID NO:1, or

(ii) a polynucleotide sequence which has at least 80% identity with the polynucleotide sequence of SEQ ID NO:1, or

(iii) a fragment of at least 75 contiguous nucleotides of the polynucleotide sequence represented by SEQ ID NO:1 having promoter activity,

wherein said isolated polynucleotide molecule is operably linked to a transcribable polynucleotide molecule."

"7. An isolated polynucleotide molecule having gene regulatory activity which

(i) comprises a polynucleotide sequence represented by SEQ ID NO:1, or

(ii) consists of a fragment of 75 to 1700 contiguous nucleotides of the polynucleotide sequence represented by SEQ ID NO:1."

III. The applicant (appellant) filed a notice of appeal and a statement setting out its Grounds of Appeal, wherein the set of claims filed with letter of 12 June 2008 was maintained.

IV. On 6 February 2013, with the summons to oral proceedings, the board sent a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) informing the appellant of its preliminary, non-binding opinion on the substantive matters of the case and introducing a new document (D7, *infra*) into the proceedings.

V. On 3 April 2013, the appellant replied to the communication of the board and filed a Main Request and a first and a second Auxiliary Request.

VI. Oral proceedings took place on 3 May 2013.

VII. Claim 1 of the **Main Request** read as claim 1 of the request before the examining division except for the fact that in part (ii) the degree of identity was of "*... at least 90% ...*" instead of "*... at least 80% ...*" and that part (iii) read as follows:

"(iii) a fragment of at least 1500 contiguous nucleotides of the polynucleotide sequence represented by SEQ ID NO:1 having promoter activity, ... (cf. Section II *supra*)"

Claim 7 of the Main Request read as claim 7 of the request before the examining division except for part (ii) which read as follows:

"(ii) consists of a fragment of at least 1500 contiguous nucleotides of the polynucleotide sequence represented by SEQ ID NO:1."

VIII. Claim 1 of the **first and second Auxiliary Requests** read as claim 1 of the Main Request except for a limitation of the feature "*... a transcribable polynucleotide molecule*" to "*... a herbicide tolerance gene*" in the last paragraph of the claim (*supra*). Claim 7 of these requests was identical to claim 7 of the Main Request.

IX. The following documents are cited in this decision:

D1: EMBL Entry AP003263, submitted 19 February 2001;

D2: WO 00/70067 A1 (publication date: 23 November 2000);

D7: R.B. Meagher et al., Trends in Genetics, July 1999, Vol. 15, No. 7, pages 278 to 284.

X. Appellant's arguments as far as relevant to the present decision can be summarized as follows:

Article 56 EPC

Although document D2, the closest prior art, referred to the family of actin genes in rice and to their regulatory regions, actin proteins were known to be very heterologous and their regulatory regions even more. Since these regions were highly heterologous among different (plant) organisms as well as within an organism such as rice, it was necessary to carry out a full screening in rice in order to identify them. The

identification, isolation and characterization of these regulatory regions was not straightforward and required substantial efforts from a skilled person.

Document D1 disclosed the specific nucleotide sequence obtained by screening a large fragment of DNA from rice. Putative regions were identified within this sequence but without providing a detailed information on their actual function. A region encoding a putative actin protein was identified but there was no disclosure of its properties let alone of those of the regulatory elements belonging to this actin gene. The less so, since it was not even known whether this putative gene was actually expressed. In order to identify these elements from the scarce information disclosed in document D1, a skilled person had to carry out substantial experiments asking for important efforts. It was not trivial to identify and characterize these regions, to find their starting and end points and how exactly they looked like, i.e. to determine their (sub)regions and the elements essential for a functional activity, in particular, for obtaining the specific expression pattern disclosed in the application. In the present case, a skilled person could only hope to succeed but there was no reasonable expectation of success.

Nothing in document D1 hinted at the advantageous expression in embryonic and reproducible tissues. The strength and tissue type in which the expression was achieved was unique. The expression pattern in female reproduction organs and developing seeds distinguished the claimed promoter from other known promoters, as

stated in the third paragraph of page 2 of the application.

XI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the Main Request or, in the alternative, the first or second Auxiliary Requests, all requests filed with a letter dated 3 April 2013.

Reasons for the Decision

Admissibility of the Main Request and of the Auxiliary Requests

1. These requests were filed on 3 April 2013 as a reply to the board's communication pursuant to Article 15(1) RPBA (cf. Section IV *supra*). Since the reasons for the refusal in the decision under appeal were only based on Articles 123(2) and 56 EPC and the board raised in its communication several objections under Articles 83 and 84 EPC, these requests can be seen as a direct reply to these objections. They do not add new subject-matter or render the case more complex but only intend to overcome the objections raised by the board. Thus, in the exercise of its discretion under Article 13(1) RPBA, the board admits them into the proceedings.

Main Request and Auxiliary Requests
Article 123(2) EPC

2. The objection raised by the examining division under this article concerned only the range of the fragment cited in claim 7 ("*... of 75 to 1700 nucleotides ...*";

cf. Section II *supra*). Since claim 7 of all requests filed on 3 April 2013 does not contain a range, this objection is no more relevant. The board has no reason to raise any other objection of its own. Thus, the requirements of Article 123(2) EPC are met.

Article 56 EPC

3. The closest prior art document D2 discloses the sequence of the 5' regulatory region of the rice actin 2 gene (SEQ ID NO:1, 2640 nucleotides; Figure 1), containing the rice actin 2 promoter (SEQ ID NO:2, 743 nucleotides) and the rice actin 2 intron (SEQ ID NO:3, 1763 nucleotides). Reference is also made in this document to the actin gene family in rice which comprises at least eight actin-like sequences per haploid genome. According to document D2, four of the rice actin coding sequences (rice actin 1, 2, 3 and 7) have been isolated and were shown to differ from each other in the tissue and stage-specific abundance of their respective transcripts. Indeed, the rice actin gene *Act1* is said to encode a transcript that is relatively abundant in all rice tissues and at all developmental stages examined. Moreover, document D2 states that a complete structural analysis of the rice *Act1* gene, including its promoter and 5' intron, is known from the prior art. It is also reported in this prior art cited in document D2 that the *Act1 5'* region is active in most, but not all, sporophytic cell types as well as in gametophytic pollen tissues which is believed to reflect an ubiquitous requirement for cytoskeletal components, such as the actin family of proteins, in plant cells (cf. page 2, line 12 to 28 of document D2).

4. Starting from this closest prior art, the technical problem to be solved is the provision of alternative rice-specific actin 5' regulatory (promoter) sequences (cf. page 4, point 2.1 of the decision under appeal).

5. As a solution to this problem, the application proposes the DNA construct according to claim 1. In view of the data shown in Tables 1 to 3 of Examples 3 and 4 of the application (bearing, respectively, the headings "*Promoter Characterization in Transient Systems*" and "*Promoter Characterization in Transgenic plants*"; cf. pages 17 to 19 of the application), the board acknowledges that the technical problem is solved by the specific embodiment of claim 1(i), i.e. the polynucleotide sequence SEQ ID NO:1 (cf. Section VII *supra*). The board is nevertheless aware that not all embodiments comprised in the claims seem to solve the technical problem. However, in view of the fact that the specific embodiment of claim 1(i) does not involve an inventive step (*infra*), the board refrains, in the present case, from discussing these other embodiments and it does not pursue some of the objections raised in the communication pursuant to Article 15(1) RPBA that may be of relevance in this regard.

6. It is also stated in document D2 that, apart from the description of the 5' regulatory regions of the rice actin 1 and actin 2 genes (the latter being disclosed in document D2), there is yet no disclosure in the prior art identifying the structure, sequence and function of the regulatory regions of other rice actin genes which nevertheless "*... could potentially provide valuable new tools for the preparation of transgenic*

plants" (cf. page 3, first paragraph of document D2). The board understands this information as a hint for a skilled person to look for, to isolate and to characterize, 5' regulatory regions of other rice actin genes.

7. Following this information given in document D2, the board is convinced that a skilled person would, as a first step, rely on data available in the prior art relating to the rice genome, such as, *inter alia*, the screening data reported in document D1 which discloses the genomic DNA sequence of chromosome 1 of rice (*Oryza sativa*). Within these data, gene P0483G10.29 is identified as encoding a putative actin protein. The skilled person is aware that, within the 5' region of the coding sequence, there may be the 5' regulatory sequences of this gene, including the 5' promoter sequence. The isolation of a large 5' fragment from the P0483G10.29 gene, the identification and its functional characterization as a 5' regulatory (promoter) sequence is considered not to require any inventive skill. Document D2 reports the presence of the structural elements in the (2.6 kbp) upstream region of the rice actin 2 gene (*Act2*), which comprises the core promoter, a non-coding exon 1 and intron 1 (cf. *inter alia*, page 8, lines 2 to 6, page 10, first paragraph, page 115, lines 5 to 11 and Figure 1 of document D2). There is ample information on general methods available in the prior art that could allow a skilled person to determine and test for a promoter activity without undue burden or inventive skill (cf. *inter alia*, page 6, last paragraph, page 7, second paragraph and page 9, line 10 to page 10, line 3 of the application; page 114, Example 1 of document D2).

8. Indeed, as noted during the examination proceedings of the application, within the 5' region of the putative actin gene identified in document D1, there is a polynucleotide sequence exhibiting 99% identity in a 1868 base pairs overlap to SEQ ID NO:1. This fact has been neither contested by the appellant in the examination proceedings nor in appeal proceedings.

9. As regards the alleged technical difficulties which, according to the appellant (cf. Section X *supra*), a skilled person would encounter when trying to identify the (sub)regions and elements within the 5' regulatory region as well as when trying to characterize those elements essential for its (promoter) function, the board notes that the application itself fails to provide a disclosure referring to any identification or characterization step. None of the (sub)regions and elements comprised within the polynucleotide sequence SEQ ID NO:1 (>1.8 kbp) is actually identified and characterized in the application. There is no information at all regarding the presence of a basal or core promoter sequence (proximal part; which in plants usually includes an initiator and TATA-box located about 40 pairs upstream of the start of transcription), the *cis*-acting motifs in the upstream promoter region (distal part; usually located 100-200 bp upstream and binding to transcription factors) or other more distant (upstream, kbp away) *cis*-acting regulatory elements (enhancers, repressors) that may also influence the stability and efficiency of the transcription and the (constitutive, cell or tissue-specific, inducible, etc.) expression pattern.

10. The appellant further argues that the specific expression pattern achieved by the polynucleotide sequence SEQ ID NO:1 provides an advantageous and unexpected effect which, in its view, justifies the acknowledgement of an inventive step (cf. Section X *supra*). The board cannot share this view for the following reasons:

10.1 Firstly, there is no evidence on file that would make it credible that the expression pattern obtained with the polynucleotide sequence SEQ ID NO:1 cannot also be obtained with a large 5' fragment of the nucleotide sequence of the actin gene disclosed in document D1 which has 99% identity in a 1868 base pairs overlap. In the absence of any evidence to the contrary, the board is convinced that the same expression pattern can reasonably be expected.

10.2 Secondly, in view of the expression patterns of the rice actin 1 and 2 genes (cf. point 3 *supra*) and those of other related plant actin genes, such as the ones of *Arabidopsis thaliana* (cf. page 280, Table 2 of document D7), the board does not share appellant's contention that the expression pattern of the polynucleotide sequence SEQ ID NO:1 is indeed unexpected and surprising.

10.3 Third, detailed data on the expression pattern of the polynucleotide sequence SEQ ID NO:1 were filed as an attachment to appellant's letter of 10 August 2009 in reply to the summons to attend the oral proceedings before the first instance. Deficiencies in these data were indicated by the board in a general manner in its communication pursuant to Article 15(1) RPBA

(cf. page 10, point 11.4 of the board's communication). Moreover, it is not evident whether comparable detailed data are derivable from the application itself, since the disclosure therein refers only to "*the regulatory elements from an actin gene*" in general (cf. page 2, line 11 to 18 of the application). However, five specific and different polynucleotide fragments from rice actin genes are disclosed (P-Os-Act15a, P-Os-Act15b, P-Os-Act16, P-Os-Act18, P-Os-Act31; SEQ ID NO:1 to 5, respectively).

10.4 Fourthly, it is also not evident that the expression pattern obtained with the polynucleotide sequence SEQ ID NO:1 is actually advantageous for the intended expression of each and every possible "*transcrible polynucleotide molecule*" (claim 1 of the Main Request, Section VII *supra*) or "*herbicide tolerance gene*" (claim 1 of the first and second Auxiliary Requests, Section VIII *supra*).

11. In view of all the above considerations, the board concludes that a skilled person trying to solve the technical problem defined in point 4 *supra*, would have arrived at a polynucleotide sequence represented by SEQ ID NO:1 in an obvious way by combining the teaching in documents D2 and D1. Accordingly, the Main Request and the first and second Auxiliary Requests do not fulfil the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski M. Wieser