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Datasheet for the decision of 23 October 2012

Case Number:	T 1499/09 - 3.3.08
Application Number:	01919367.1
Publication Number:	1263968
IPC:	C12N 15/54

Language of the proceedings: EN

Title of invention: Beta 1.2-xylosyltransferase-gene from Arab

Beta 1,2-xylosyltransferase-gene from Arabidopsis

Patent Proprietor: Glössl, Josef

Opponent: Harrison Goddard Foote

Headword: Xylosyltransferase/GLÖSSL

Relevant legal provisions:

EPC Art. 54, 56, 83, 84, 113(1), 123(2)(3) EPC R. 80 RPBA Art. 13(1)(3)

Keyword:

"New main request - compliance with Rule 80 EPC (yes)" "Added matter (no)" "Extension of the scope of protection (no)" "Sufficiency of disclosure, novelty and inventive step (yes)" "Article 113(1) EPC - complied with"

Decisions cited:

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Catchword:



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Beschwerdekammern

Boards of Appeal

Chambres de recours

Case Number: T 1499/09 - 3.3.08

D E C I S I O N of the Technical Board of Appeal 3.3.08 of 23 October 2012

Appellant: (Patent Proprietor)	Glössl, Josef Zentrum für Angewandte Genetik Universität für Bodenkultur Wien, Muthgasse 18 AT-1190 Vienna (AT)
Representative:	Alge, Daniel Sonn & Partner Patentanwälte Riemergasse 14 AT-1010 Wien (AT)
Respondent: (Opponent)	Harrison Goddard Foote Belgrave Hall Belgrave Street Leeds LS2 ODD (GB)
Representative:	Williams, Richard Andrew Norman Harrison Goddard Foote 8th Floor 140 London Wall London EC2Y 5DN (GB)
Decision under appeal:	Decision of the Opposition Division of the European Patent Office posted 30 March 2009 revoking European patent No. 1263968 pursuant to Article 101(3)(b) EPC.

Composition of the Board:

Chairman:	Μ.	Wieser		
Members:	М.	R.	Vega	Laso
	J.	Geschwind		

Summary of Facts and Submissions

- I. The appeal lies from the decision of the opposition division posted on 30 March 2009 revoking the European patent No. 1 263 968 with the title "Beta 1,2-xylosyltransferase-gene from Arabidopsis" under Article 101(3) (b) EPC. The patent at issue is based on European patent application No. 01919367.1 which was filed as international application under the PCT and published as WO 01/64901 (in the following "the application as filed"). The patent was granted with 20 claims.
- II. The opposition to the grant of the patent was based on the grounds for opposition mentioned in Article 100(a), (b) and (c) EPC, in particular that the claimed subject-matter lacked novelty (Article 54 EPC), inventive step (Article 56 EPC) and industrial application (Article 57 EPC), that the granted claims encompassed subject-matter which went beyond the content of the application as filed, and that the claimed invention was not disclosed in a manner sufficiently clear and complete for a person skilled in the art to carry it out.
- III. In the decision under appeal, the opposition division found that Article 100(c) EPC prejudiced the maintenance of the patent as granted (main request), that the amendments introduced into the claims of the first auxiliary request then on file contravened Article 123(3) EPC, and that the subject-matter of the claims according to the second and third auxiliary requests then on file lacked novelty and inventive step, respectively.

- IV. Together with the statement of grounds of appeal, the patent proprietor (appellant) submitted additional evidence and four sets of claims as first to fourth auxiliary requests replacing the previous auxiliary requests. Maintenance of the patent as granted remained his main request. As a subsidiary request, oral proceedings were requested.
- V. The opponent (respondent) submitted observations on the statement of grounds of appeal and requested oral proceedings.
- VI. The appellant replied and put forward additional arguments.
- VII. The parties were summoned to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons to oral proceedings, the board expressed its provisional opinion on some of the issues to be discussed, in particular issues in connection with Articles 123(2), 54 and 56 EPC. In view of the new evidence and requests filed by the appellant in appeal proceedings, the board drew attention to Article 12(4) RPBA.
- VIII. In response to the board's communication, the appellant submitted a further amended set of claims as new auxiliary request 1b.
- IX. By letter of 27 September 2012, the respondent withdrew its request for oral proceedings and informed the board

that it would not be attending the scheduled oral proceedings.

- X. During the oral proceedings held on 23 October 2012, in which the respondent was not represented, the appellant filed amended claims 1 to 17 as his new main request.
- XI. Amended claims 1, 10 and 11 of the new main request read:

"1. An isolated DNA molecule characterised in that it codes for a plant protein having β 1,2-xylosyl-transferase activity and in that it comprises a sequence selected from the group consisting of

- a sequence SEQ ID NO 8 with an open reading frame from base pair 227 to base pair 1831,
- a sequence which is at least 70% identical with SEQ ID NO: 8,
- a sequence which is complementary to SEQ ID NO: 8;

with the proviso that a DNA sequence as disclosed in EP 1 033 405 A2 under SEQ ID NO 77276 translated to an amino acid sequence according to SEQ ID NO 77277 of EP 1 033 405 A2 is excepted.

10. A method of preparing recombinant host cells, particularly plant cells, or plants, wherein the production of β 1,2-xylosyltransferase is suppressed or completely stopped, characterised in that the vector according to claim 7 is inserted into said host cell or plant, respectively.

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11. A method of preparing recombinant host cells, particularly plant cells or plants, respectively, characterised in that the DNA molecule according to any one of claims 1 to 5 with a deletion, insertion and/or substitution mutation is inserted into the genome of said host cell or plant, respectively, at the position of the non-mutated, homologous sequence, wherein the production of β 1,2-xylosyltransferase is suppressed or completely stopped."

Dependent claims 2 and 3, which are derived from claim 3 as granted, and dependent claims 4 and 5, which are identical to the corresponding claims of the patent as granted, relate to particular embodiments of the DNA molecule according to claim 1. Independent claims 6 and 7 relate to biologically functional vectors and are identical to claims 8 and 9 of the patent as granted. Independent claims 8 and 9, which are identical to claims 11 and 12 of the patent as granted, concern a method of preparing a cDNA and a method of cloning a β l,2-xylosyltransferase, respectively. Claim 12, which has been amended to adapt the reference to the numbering of the previous claims, is directed to recombinant plants or plant cells prepared by a method according to claims 10 or 11. Claims 13 to 17 are identical to claims 16 to 20 of the patent as granted, except for the references being adapted to the new numbering. Claims 6, 7 and 10 of the patent as granted have been deleted.

- (1): WO 99/29835, published on 17 June 1999;
- (2): EMBL databank, Accession No. AB015479, created on 19 June 1998;
- (8): S. Pagny et al., 2003, The Plant Journal,Vol. 33, pages 189 to 203;
- (9): P. Bencúr et al., 2005, Biochem. J.,Vol. 388, pages 515 to 525;
- (11): H. Puchta, 2002, Plant Molecular Biology, Vol. 48, pages 173 to 182;
- (12): T. Mengiste and J. Paszkowski, July/August 1999, Biol. Chem., Vol. 380, pages 749 to 758;
- (13): R. Terada et al., October 2002, nature biotechnology, Vol. 20, pages 1030 to 1034;
- (16): R. Strasser et al., 2000, FEBS Letters, Vol. 472, pages 105 to 108;
- Annex 1: Results of a search of nucleic acid sequence libraries available prior to 3 March 2000 using the partial cDNAs described in document (1) (SEQ ID NOs: 6 and 7);

Annex 5: Nucleotide alignment of SEQ ID NOs: 6 and 7 of document (1) with SEQ ID NO: 8 of the patent;

Annex VII: S. A. Kempin et al., 23 October 1997, Nature, Vol. 389, pages 802 and 803;

Annex VIII: M. Hanin et al., 2001, The Plant Journal, Vol. 28, No. 6, pages 671 to 677.

XIII. The submissions made by the appellant may be summarized as follows:

Admission of the new main request into the proceedings

The new set of amended claims did not give rise to additional issues, but overcame objections under Article 123(2) EPC on which the board had expressed an adverse provisional opinion. The amendments were straightforward and did not require further discussion.

Article 123(2) EPC

Amended claim 1 had a basis in claims 1, 2 and 3 of the application as filed. Replacing the wording "above sequence" in the original claim 1 by "SEQ ID NO: 8" did not introduce subject-matter extending beyond the content of the application as filed. It was absolutely clear to the skilled person reading the application as filed that "homology" in the context of a quantitative measure meant "identity".

Claim 11 had a basis in original claim 14. The reference to the omitted claim 6 was replaced by the

features of this claim. The additional feature "wherein the production of $\beta 1, 2$ -xylosyltransferase is suppressed or completely stopped" had a basis in claim 15 of the application as filed.

Article 123(3) EPC

The wording "(sequence A)", which had been introduced into claim 1 as granted to define different sequence variants (50% identical, hybridizing sequence, genetic code degenerated sequence), served only as a placeholder for the phrase "SEQ ID NO: 8 with an open reading frame from base pair 227 to base pair 1831". Thus, deleting this wording or replacing it by "SEQ ID NO: 8" did not extend the scope of protection conferred by the patent as granted.

Article 83 EPC

It was possible for a skilled person to modify the SEQ ID NO: 8 to obtain a sequence which still encoded active β l,2-xylosyltransferase. The activity could be tested in an assay as described in the application.

The insertion of a given sequence into a plant genome, in particular by homologous recombination was well understood at the priority date and described in the application. Even though the application provided only a reference to a method for gene targeting in the moss *Physcomitrella patens* (see page 16, third full paragraph, lines 5 and 6 of the application), the same method could be applied to the transformation of other plants. Annexes VII and VIII showed successful gene targeting methods in *Arabidopsis*. Low transformation frequency in higher plants was not a serious obstacle because successful recombination events could be screened as described in the application. Thus, the requirements of Article 83 EPC were met.

Article 54 EPC

The subject-matter of claim 1 was novel over document (2). This document was not prior "art" because it did not contain a technical teaching with regard to the enzymatic activity. Since the document did not provide an enabling disclosure, a DNA molecule encoding a xylosyltransferase was not made available to the public.

Article 56 EPC

Document (1) represented the closest state of the art. The invention claimed in the patent differed from the teachings in document (1) in that the patent provided a full-length sequence encoding an active xylosyltransferase whereas document (1) did not. Moreover, while document (1) related to a soybean xylosyltransferase, the patent provided a sequence that encoded an *Arabidopsis thaliana* xylosyltransferase.

The objective technical problem was the provision of a full-length nucleotide sequence that encoded an active plant β 1,2-xylosyltransferase. A person skilled in the art could have tried to obtain the full-length sequence coding for the soybean xylosyltransferase by using the partial sequence provided in Figure 10 of document (1) to clone the xylosyltransferase gene from a soybean library. However, there was no evidence on file that

this approach would have been successful, nor that the skilled person would have arrived at a sequence which fell under the scope of claim 1.

The opposition division's assumption that the skilled person would have relaunched a BLAST search was speculative. The skilled person *could* possibly have done so, but it was a completely unproven allegation without any support in document (1) that this *would* have been obvious. Moreover, it had not been proven that the skilled person could have found document (2) in a BLAST search. Even though this document was in principle available at the priority date, the authors of document (1) had not been able to find any homologous sequences in a BLAST search (see statements on page 6, lines 19 and 20 of document (1)).

Document (1) did not describe a single xylosyltransferase protein, but two different soybean proteins which were not related to each other (see page 23, lines 1 to 3). Although the sequence of three peptides from the 56 kDa protein and two peptides from the 59 kDa protein was provided, document (1) did not describe any primers based on the peptide sequences, nor did it provide any incentive to try to use such primers in an amplification reaction with *Arabidopsis* mRNA instead of soybean mRNA. In any case, it had not been proven that such amplification reactions would have identified the claimed DNA molecule.

The results of the search presented in Annex 1 did not represent what the skilled person would have found at the priority date because sequence database entries created or modified after that date were retrieved. Thus, Annex 1 was artificial and without any probative value. Nor could the examples of the patent itself serve as evidence of what the skilled person would have retrieved from a BLAST search. The search that led to the isolation of the *Arabidopsis* xylosyltransferase gene had been done using a combination of one peptide of the 56 kDa protein and a truncated version of a peptide of the 59 kDa protein. The skilled person would not have taken this course of action which deviated from the routine practice.

Moreover, retrieving a hit in a BLAST search was not sufficient to provide the present invention. Generating a true cDNA sequence from an unannotated genomic clone was far from trivial. *In silico* methods did not recognise reliably the correct start and stop codons. Without the knowledge of the correct gene structure, the skilled person would have encountered difficulties designing amplification primers to obtain the xylosyltransferase cDNA.

Starting from the cDNA sequences provided in document (1) (SEQ ID NOS: 6 and 7) the skilled person had no reasonable expectation of success. Since all three reading frames of SEQ ID NO: 6 contained stop codons, the skilled person would not have expected this sequence to encode a xylosyltransferase protein. Thus, inventive step should be acknowledged.

XIV. The submissions by the respondent in writing were essentially as follows (N.B. The respondent did not attend the oral proceedings during which the new main request was filed. Thus, the objections made in writing to corresponding subject-matter of the previous requests are reported hereinafter):

Article 123(2) EPC

The decision under appeal was deficient because the opposition division failed to reach a formal decision on each of the objections raised under Article 123(2) EPC.

Each of claims 1 and 3 as originally filed claimed sequences of a numerical percentage <u>homology</u> with <u>SEQ</u> <u>ID NO: 8</u>. There was no basis in the application as filed for sequences being <u>percentage identical</u> to the reference sequence. Since "identity" and "homology" neither had the same meaning nor were calculated or estimated by the same methods, there was a reasonable doubt that the amendment of the claims to read "identical" altered the meaning or scope of the original claims and, consequently offended against Article 123(2) EPC.

Moreover, the addition of the wording "... selected from the group consisting of ..." to claim 1 restructured the original claim 1 so that the range of sequences which the reference DNA molecule is "comprised of" was broadened. DNA molecules which comprised a sequence at least 70% identical with SEQ ID NO: 8 were not encompassed by the original claim 1.

Articles 84 and 123(3) EPC

Claim 11, which was directed to a method of preparing recombinant host cells, had been amended to refer back

to the DNA molecule of any of claims 1 to 5 with the additional requirement of a deletion, insertion and/or substitution mutation. Contrary to the requirement in claims 1 to 5, less than full length sequences not encoding β l,2-xylosyltransferase activity could be used in the claimed method. Because of uncertainty over the requirement for encoding a protein with xylosyl-transferase activity, the claim lacked clarity within the meaning of Article 84 EPC and it could be reasonably assumed that the amendment resulted in a broadening of the scope of protection conferred by the patent, contrary to Article 123(3) EPC.

Article 83 EPC

Claim 1 and claims dependent or referring to claim 1 lacked enablement contrary to Article 83 EPC. The specification as originally filed did not identify or describe the essential elements of the amino acid or nucleotide sequences of the β l,2-xylosyltransferase that were responsible for the xylosyltransferase activity. The average skilled person was therefore left in the dark as to the nature and extent of the changes that could be made to the SEQ ID NO: 8 whilst preserving the enzyme activity.

While document (8) provided some guidance as to where deletions could be made in the N-terminal region of the β l,2-xylosyltransferase, neither this document nor document (9) enabled the average skilled person to provide DNA molecules with a deletion, substitution or insertion mutation as specified in claim 11. Moreover, while claim 11 required homologous recombination, the application failed to describe any generally applicable method of homologous recombination in higher plants, let alone specific methods to individual groups of plants at lower taxonomic levels. As indicated in documents (11), (12) and (13), at the filing date of the priority application as well as of that of the application homologous recombination was not enabled in all plants. Thus, claim 11 lacked enablement contrary to Article 83 EPC.

Article 56 EPC

The opposition division's finding of lack of inventive step with regard to the auxiliary request 3 then on file was correct and applied equally to the present requests. Document (1) was the acknowledged closest prior art document. It described two very similar, related xylosyltransferase proteins and suggested commonality via gene splicing (see passages on page 9, lines 2 and 3; page 22, line 29 to page 23, line 3; page 32, line 29 to page 33, line 5; and page 33, line 24 to page 34, line 1). On page 35, lines 19 to 26 it was suggested to prepare oligonucleotides from the peptide sequences provided therein and use them to clone the gene for the xylosyltransferase gene from a soybean library. Document (1) also referred repeatedly to the activity of carrying out a BLAST search (see page 6, lines 19 and 20; page 9, lines 3 to 5; page 23, lines 5 to 8; and page 34, lines 1 to 4).

The sole technical difference between the claims and document (1) was the provision of a nucleotide sequence that encoded an active xylosyltransferase. The objective technical problem was the provision of the clones and of the sequenced whole gene of a plant xylosyltransferase.

The opposition division had been entirely correct to decide that the average skilled person, starting with the peptide sequences of document (1), would have carried out BLAST searches, because this was the easiest and most efficient way of finding full length and/or highly related protein sequences in the public databases. Additionally, the skilled person would have been motivated to do it because it would have known about the Arabidopsis sequencing project and how it was nearing completion. The result of the obvious BLAST searching was not just finding the genomic sequence of document (2), but also identifying the sequence, in particular the coding sequence of the xylosyltransferase gene within that genomic DNA clone using tools available at the priority date. Once the gene sequence had been identified, no inventive effort or undue burden was required for expressing the gene product and testing it for xylosyltransferase activity.

Since document (1) made available a partial clone with the SEQ ID NOS: 6 and 7, it was an obvious step to use the partial sequences to screen a cDNA library of any plant, not just soybean. Routine methods would have been used. The skilled person would not be confused by the presence of "stop" codons in all three reading frames of the SEQ ID NO: 6, as it would be clear that the SEQ ID NOs: 1 to 5 obtained from sequencing the peptides represented the correct amino acid sequence of the xylosyltransferase. As an alternative approach, the skilled person would have been able to repeat the purification procedure of document (1) and generate sufficient full length protein to sequence it and carry out a BLAST search. Another option had been to generate antibodies to the purified soybean xylosyltransferase and use them to screen a cDNA library of *Arabidopsis*.

Whichever of the routine approaches the skilled person might have selected, there would always have been a reasonable expectation of success in being able to isolate and clone a full length cDNA from a library. There was <u>no evidence</u> to prove the alleged technical difficulties when trying to obtain a full length cDNA clone from soybean. Both the patent and document (16) published by the inventors were silent on any technical difficulties, and described cloning of the *Arabidopsis* xylosyltransferase applying only routine genomic analysis and ordinary methods of cloning and expression.

- XV. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of claims 1 to 17 of the new main request filed during oral proceedings and an amended description adapted thereto.
- XVI. The respondent (opponent) requested in writing that the appeal be dismissed.

Reasons for the Decision

Admission of the new main request into the proceedings

- 1. According to Article 13(1) RPBA, any amendment to a party's case after it has filed its grounds of appeal or reply may be admitted and considered at the board's discretion. Although the submission of the claims at the oral proceedings must be regarded as a "very late" submission which should be accepted and considered only in exceptional situations, in the present case the amendments introduced into the claims address issues under Articles 123(2)(3), 83, 54 and 56 EPC which were either decided by the opposition division to the appellant's disadvantage, or raised by the board in its communication.
- 2. The board has decided to admit the amended claims of the new main request into the proceedings. In exercising its discretion, the board has taken into account that the introduced amendments are straightforward, neither raise new issues nor take the other party by surprise, and can be dealt with without adjournment of the oral proceedings (see Article 13(3) RPBA).

Rule 80 EPC

3. Amended claim 1 according to the new main request (see paragraph XI above) differs from the corresponding claim as granted in that the protein encoded by the claimed DNA molecule is now characterised as a "*plant protein*", that the wording "*sequence* A" has been omitted from the first element of the group of

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sequences specified in the claim, that the second element of the group is defined as "a sequence which is at least 70% identical with SEQ ID NO: 8" (instead of "a sequence which is at least 50% identical with said sequence A" as in claim 1 as granted), and that the wording "complementary to any of the above sequences" has been substituted by the wording "complementary to SEQ ID NO: 8". The board is satisfied that the amendments introduced into claim 1 are occasioned by grounds for opposition under Article 100(b) and (c) EPC.

4. Moreover, the board is convinced that the amendments introduced claim 10, which is derived from claim 13 as granted, and claim 11, which is derived from claim 14 as granted, have been occasioned by the ground for opposition under Article 100(b) EPC. Thus, the requirement of Rule 80 EPC is fulfilled.

Article 123(2) EPC

- 5. Claim 1 of the new main request is identical to the corresponding claim according to the third auxiliary request underlying the decision under appeal, except that the protein encoded by the claimed DNA molecule is characterised by the additional feature "*plant* [protein]" (see paragraph XI above).
- 6. In the decision under appeal, the opposition division found that the amendments introduced into the claims of the third auxiliary request then on file did not offend against Article 123(2) and (3) EPC (see paragraph II.2.3 of the decision under appeal). This finding has been contested by the respondent (see paragraph XIV above).

7. In respect of Article 123(2) EPC, the respondent argued that the wording "... % identical with ... " had no basis in the application as filed. In fact, only the wording "... % homologous with ... " is used in the application as filed. However, in the board's view a person skilled in the art reading the application understands that, when the degree of similarity of two nucleotide sequences is expressed quantitatively as a percentage number, "homologous" and "identical" have the same meaning, namely the ratio between the number of identical nucleotides and the total number of nucleotides. Contrary to the respondent's view, in the context of a quantitative comparison of nucleotide sequences by alignment, the terms "% homologous" and "% identical" cannot be interpreted or estimated differently, as it may be done when comparing amino acid sequences.

8. The respondent argued further that by amending claim 1 to read "... selected from the group consisting of ... a sequence which is at least 70% identical with SEQ ID NO: 8", subject-matter which extended beyond the content of the application as filed had been added. The board disagrees with this view. In spite of a certain ambiguity in the language of claim 1 of the application as filed, a person skilled in the art would not understand the phrase "... is at least 50% homologous with ..." as referring to the "DNA molecule", but rather to the term "a sequence", because only in the context of comparing two sequences a degree of similarity can be expressed. 9. The subject-matter of claim 1 has a basis in claims 1, 2 and 3 of the application as filed. In particular, the feature "plant protein" introduced into the amended claim is disclosed in the original claim 1. The board is thus convinced that the amendments introduced into claim 1 do not contravene Article 123(2) EPC.

Articles 84 and 123(3) EPC

- 10. The respondent raised an objection under Articles 84 and 123(3) EPC against the amendments introduced into claim 11 to define the DNA molecule by reference to claims 1 to 5 (instead of claim 6 as in claim 14 as granted), and to include the additional requirement of a deletion, insertion and/or substitution mutation.
- Amended claim 11 is derived from claim 14 of the patent 11. as granted by incorporating the wording of claim 6 as granted, which has now been deleted in the set of claims according to the new main request. The board does not share the respondent's view that there is an ambiguity as to whether or not claim 11 requires that the encoded protein has β l, 2-xylosyltransferase activity. It is clear that, by virtue of the reference to claims 1 to 5, the features defining the DNA molecules according to each of the claims 1 to 5 are incorporated into claim 11, and there is no contradiction between these features and the requirement of a deletion, insertion and/or substitution mutation, because this requirement does not necessarily lead to the encoded protein losing the β l, 2-xylosyltransferase activity.

12. No further objections under Article 84 and/or 123(3) EPC were raised by the respondent, and the board sees no reason for raising any of its own motion. Thus, the claims are regarded as complying with the clarity requirement, and the amendments introduced are considered not to extend the protection conferred by the patent as granted.

Article 83 EPC

- 13. While in its communications in preparation of the oral proceedings the opposition division expressed a provisional opinion on Article 83 EPC favourable to the patent proprietor (the present appellant), in the decision under appeal the division did not deal with the objections of lack of sufficient disclosure and revoked the patent on the grounds of lack of inventive step.
- 14. The objections raised by the respondent in appeal proceedings fail to convince the board that the requirements of Article 83 EPC are not fulfilled. As regards the objection raised by the respondent to claim 1, the board observes that, at the priority date, the approach followed in the cited documents, namely post-published documents (8) and (9), was a well-known approach used for studying the structural requirements for a given enzyme activity. Making serial deletions in the claimed DNA molecule and testing the β l, 2-xylosyltransferase activity of the encoded protein in order to find out which regions of the protein are essential for the enzymatic activity was part of the knowledge of an average person skilled in the art at the priority date, and did not require an undue amount

of experimentation or inventive ingenuity. Thus, in the board's view the cited documents do not support, but rather refute the respondent's allegation that a person skilled in the art was left in the dark as to how to modify the SEQ ID NO: 8 whilst preserving the enzyme activity.

- 15. As concerns the objection to claim 11, it is true that at the priority date methods for gene targeting in higher plants by homologous recombination known in the art were rather inefficient, particularly when foreign DNA was integrated (see abstract of document (12)). However, the board believes that, albeit with low recombination frequencies, a skilled person would have been able to obtain recombinant plant cells by disrupting a genomic sequence with a mutated homologous sequence, as specified in claim 11. In the board's view, the evidence cited by the respondent does not support its allegation of lack of enablement. On the contrary, document (13) describes efficient gene targeting by homologous recombination in rice (see title). Apart from indicating that targeting frequencies in higher plants are low, document (12), which reviews the knowledge on the mechanisms by which homologous recombination takes place in plants, does not prove that homologous recombination was not enabled at the priority date. The same is true for document (11).
- 16. In view of the above, the board concludes that the invention claimed in claims 1 and 11 is sufficiently disclosed within the meaning of Article 83 EPC.

Article 54 EPC

- 17. In the decision under appeal, the opposition division found that the subject-matter of the claims according to the third auxiliary request then on file was novel, in particular in view of document (2). Since claim 1 of the new main request is - except for the additional feature "plant [protein]" - identical to the corresponding claim according to the third auxiliary request underlying the decision under appeal, this finding would apply also to the present claim 1.
- 18. The board shares the view of the opposition division that document (2), which describes a genomic sequence from chromosome 5 of Arabidopsis thaliana, does not anticipate the subject-matter of claim 1. Although this unannotated sequence having 80675 base pairs includes sequences encoding the β 1,2-xylosyltransferase of Arabidopsis, the coding sequence is interrupted by introns which are not specifically identified in the document. Thus, an isolated molecule as claimed in claim 1 cannot be derived, directly and unambiguously, from document (2).
- 19. The objections of lack of novelty raised by the respondent in its reply to the statement of grounds of appeal concerned either variants of the DNA molecule of claim 1 which are no longer claimed, or the subjectmatter of claim 6 as granted which has been deleted in the set of claims according to the present main request.
- 20. Hence, the subject-matter of the claims of the main request is considered to be novel.

Article 56 EPC

- 21. The opposition division found in respect of the third auxiliary request then on file that the subject-matter of claims 1 and 10 was "partly" obvious in view of document (1) alone, and "partly" obvious in view of document (1) in combination with document (2). Consequently, these claims were found to lack an inventive step within the meaning of Article 56 EPC. Claims 1 and 10 of the present main request are - except for the additional feature "*plant*" in claim 1 - identical to the corresponding claims of the third auxiliary request in opposition proceedings.
- 22. It is undisputed that document (1), which describes the purification of a β l,2-xylosyltransferase from soybean, represents the closest state of the art. Two proteins having, respectively, 56 kDa and 59 kDa were isolated from soybean seeds and identified as β l, 2-xylosyltransferases. Because of similarities in the peptide map obtained by Endo lys C digestion of each protein, it is suggested in document (1) that the two proteins may have arisen from gene splicing (see Example 13, paragraph bridging pages 33 and 34). After digestion of the purified proteins, several peptides were isolated and sequenced (see amino acid sequences in Figure 4), and a BLAST search was run with the partial amino acid sequences obtained from the two proteins. However, the sequences "... did not show strong identity or homology to sequences from other known proteins ... " (see page 34, lines 1 to 4 and page 6, lines 19 and 20). In the passage on page 35, lines 19 to 21, it is suggested that oligonucleotides could be prepared from the peptide sequences and used "... to clone the gene for

this enzyme [the xylosyltransferase] from a soybean
library".

- 23. The parties also agree in that, starting from document (1), the problem to be solved was the provision of a full-length nucleotide sequence that encoded an active plant β 1,2-xylosyltransferase. It has not been disputed by the respondent that the DNA molecule claimed in claim 1 indeed solves this problem.
- 24. The issue in dispute is whether or not the subjectmatter of this claim was obvious to a person skilled in the art at the relevant date.
- 25. In the board's view, the person skilled in the art reading document (1) had no reason to doubt that, if any proteins showing homology to the peptide sequences described in document (1) had been known at the time the BLAST search was run, they would have been found. Thus, the skilled person would have assumed that, in fact, no homologous sequences were available and, consequently, would have tried to clone the βl,2-xylosyltransferase gene following the suggestion in document (1), i.e. by preparing oligonucleotides from the described peptides and using them to screen a soybean library for the desired gene.
- 26. Document (1) describes two different proteins with xylosyltransferase activity which, although quite similar, contain enough differences to indicate that the smaller protein may not be processed directly from the larger by removal of a peptide (see page 33, lines 26 to 28). Three peptides derived from the 56 kDa protein and two derived from the 59 kDa protein are

described in the document, but no specific guidance is provided as to which oligonucleotides or combination of oligonucleotides prepared from one or more peptides from either protein would be more suitable for cloning a xylosyltransferase gene. Hence, the skilled person would have had to try oligonucleotides or combinations of oligonucleotides derived from different peptides, but had a reasonable expectation of succeeding in finding a xylosyltransferase gene in a soybean library.

- 27. Whilst it could be accepted that, following the approach suggested in document (1) the skilled person may have succeeded in cloning the soybean xylosyltransferase gene, this does not mean that, by isolating a DNA molecule including the soybean xylosyltransferase sequence, the skilled person would have arrived at a DNA molecule according to claim 1. It is apparent from Figure 11 of the patent that the soybean xylosyltransferase protein and the protein from Arabidopsis thaliana show little similarity in the amino acid sequence, and Annex 5 filed by the present respondent in opposition proceedings shows that SEQ ID NOs: 6 and 7 of document (1), which are said to be partial cDNA sequences of the soybean xylosyltransferase gene, show, respectively, 68% and 68.7% identity to the SEQ ID NO: 8 of the invention. Claim 1 however requires at least 70% identity to the SEQ ID NO: 8.
- 28. In view of the above, the board is not convinced that, starting from document (1) and following the suggestions provided therein, it was obvious to the skilled person to arrive at the DNA molecule of claim 1.

29. In the decision under appeal, the opposition division held that a person skilled in the art would have relaunched a BLAST search using the sequences provided in document (1) on a regular basis. He/she would have found document (2) describing a genomic Arabidopsis clone comprising the entire $\beta 1, 2$ -xylosyltransferase sequence.

- 30. In the board's view, the opposition division's finding is tainted with hindsight. As stated above, in view of the statements in document (1) there was no reason for the skilled person to run another BLAST search. But even if he/she had done so, it cannot be said with certainty that he/she would have found the clone with the sequence specified in document (2). The fact that the present inventors found this clone in a search using oligonucleotides from the peptides of document (1), is not regarded by the board as being prejudicial to inventive step, because the specific combination of oligonucleotides used by the inventors was not disclosed in document (1), nor is there any evidence on file that, using any oligonucleotide of document (1), alone or in any combination, the clone of document (2) would have been retrieved.
- 31. Summarising the above, the board concludes that finding the DNA molecule of claim 1 was not obvious to a person skilled in the art. The same applies to the method of claim 10, in which a vector comprising the DNA molecule of claim 1 in inverse orientation is used.

Conclusion

32. Claims 1 to 17 according to the new main request and the invention to which they relate, meet the requirements of the EPC.

Article 113(1) EPC - Right to be heard

33. In its communication under Article 15(1) RPBA, the board provided some observations with the aim of helping the parties to prepare for the oral proceedings. It also expressed a provisional opinion on some of the issues to be discussed. The parties were given the opportunity to present their comments. However, the respondent did not reply to the board's observations, but withdrew its request for oral proceedings and did not attend the oral proceedings. Even though the present decision is taken on a set of amended claims which was filed during the oral proceedings, the board believes that both parties had ample opportunity to file any observations they wished in respect of the grounds and evidence on which this decision is based. Thus, the board is satisfied that the provisions of Article 113(1) EPC are complied with.

Order

For these reasons it is decided that:

- 1. The decision under appeal is set aside.
- 2. The case is remitted to the department of first instance with the order to maintain the patent in the following form:
 - claims 1 to 17 of the main request filed at the oral proceedings,
 - amended pages 3 to 11 of the description filed at the oral proceedings, and pages 12 to 20 of the description of the patent as granted,
 - figures 1 to 11 of the patent as granted.

The Registrar:

The Chairman:

A. Wolinski

M. Wieser